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Symposium on Arteriosclerosis

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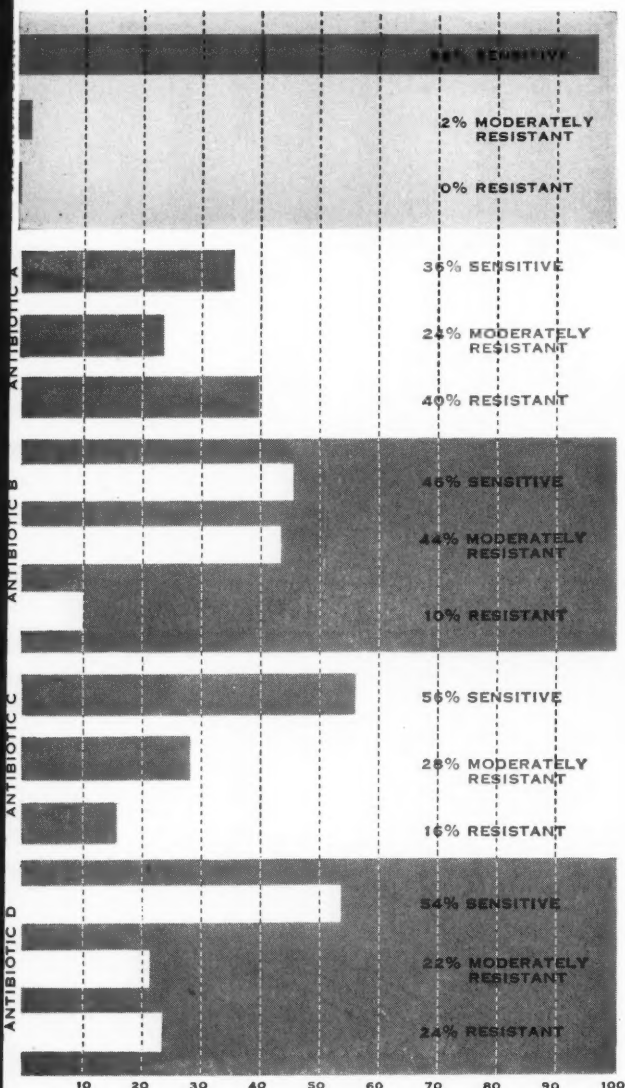
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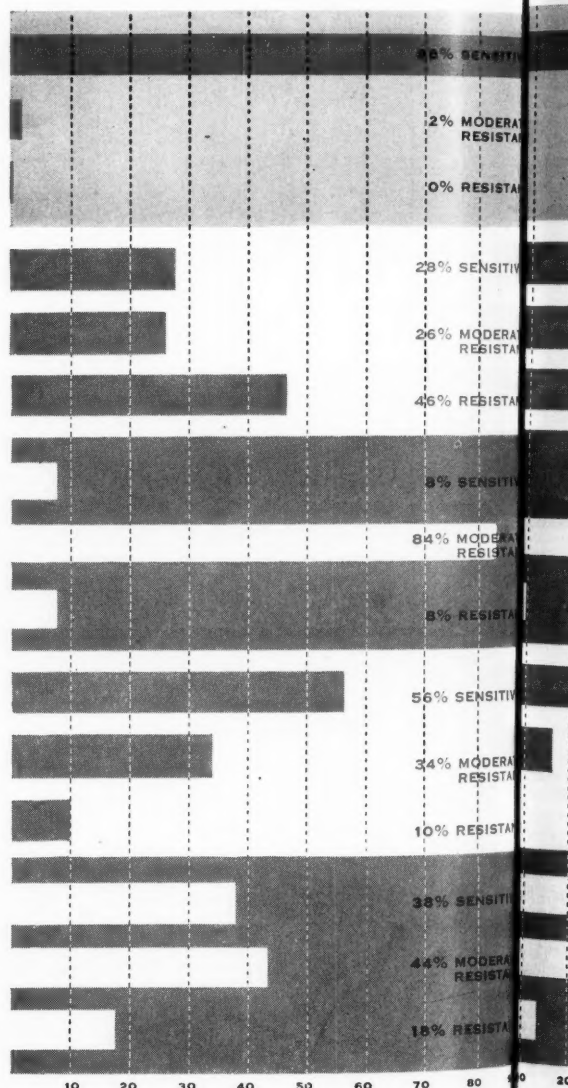
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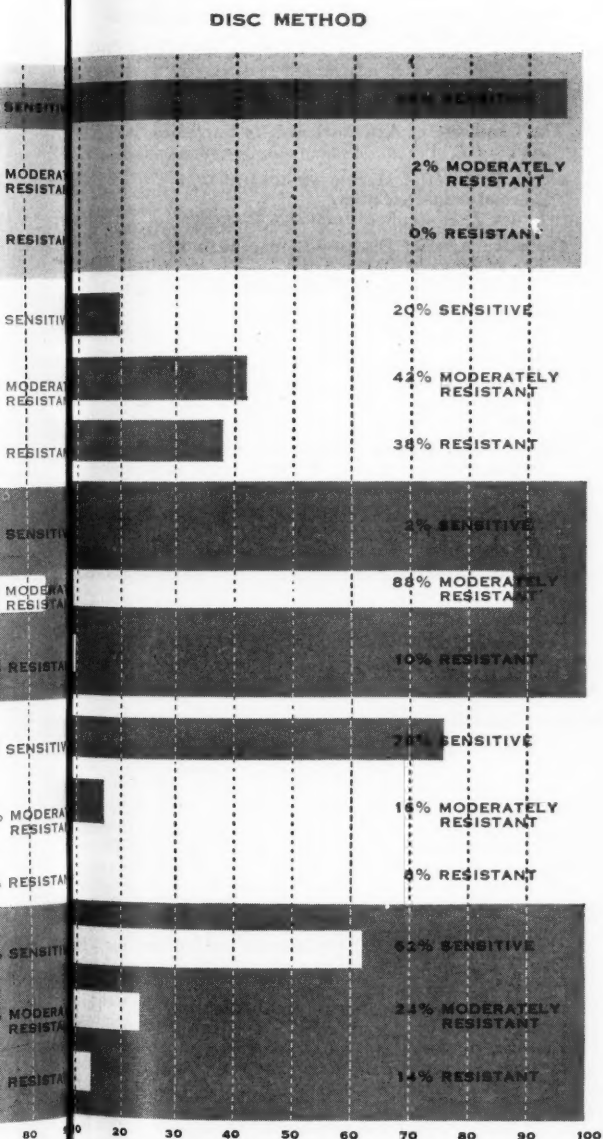


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References: (1) Spink, W. W.: *Arch. Int. Med.* 94:167, 1954. (2) Finland, M.: *J.A.M.A.* 158:188, 1955. (3) Tebrock, H. E., & Young, W. N.: *New York J. Med.* 55:1159, 1955. (4) LeMaistre, C.: *M. Clin. Nor. America* 39:899, 1955. (5) Kagan, B. M.: *J.M.A. Georgia* 44:210, 1955. (6) Branch, A.; Starkey, D. H.; Rodgers, K. C., & Power, E. E., Welch, H., & Marti-Ibañez, F.: *Antibiotics Annual, 1954-1955*, New York, Medical Encyclopedia, Inc., 1955, p. 1125. (7) Kutscher, A. H.; Seguin, L.; Lewis, S.; Piro, J. D.; Zegarelli, E. V.; Rankow, R., & Segal, R.: *Antibiotics & Chemother.* 4:1023, 1954. (8) Weil, A. J., & Stempe, B.: *Antibiotic Med.* 1:319, 1955. (9) Jones, C. P.; Carter, B.; Thomas, W. L., & Creadick, R. N.: *Obst. & Gynec.* 5:365, 1955.

Adapted from Branch, Starkey, Rogers & Power\*



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# Minnesota

## Contents for December

### SCIENTIFIC ARTICLES

#### SYMPOSIUM ON ARTERIOSCLEROSIS

##### Peripheral and Cerebral Arteriosclerosis

- Clinical Aspects of Occlusive Arteriosclerosis of the Extremities**  
*A. Wilbur Duryee*, New York, New York..... 829
- Clinical Aspects of Arteriosclerotic Aneurysm and Arteriosclerotic Occlusion of the Abdominal Aorta**  
*Edgar A. Hines, Jr.*, Rochester, Minnesota..... 836
- Clinical Picture of Cerebral Arteriosclerosis**  
*C. Miller Fisher*, Boston, Massachusetts..... 839

##### The Internist and Some Tools

- Arteriosclerosis in African Populations**  
*John F. Brock and B. Bronte-Stewart*, Cape Town, South Africa ..... 852
- Treatment of Hypercholesterolemia**  
*Haqvin Malmros and Gerhard Wigand*, Lund, Sweden ..... 864
- Electrocardiogram in Coronary Heart Disease**  
*Ernst Simonson*, Minneapolis, Minnesota..... 871
- Quantitative Electrocardiography**  
*Elliot V. Newman*, Nashville, Tennessee..... 874
- Ballistocardiogram in the Diagnosis of Coronary Atherosclerosis**  
*Wm. R. Scarborough*, Baltimore, Maryland..... 880

##### Medical Emergencies in Myocardial Infarction

*E. Cowles Andrus*, Baltimore, Maryland ..... 880

##### Evaluation of Status and Results of Management in Coronary Heart Disease

*Henry I. Russek*, Staten Island, New York..... 891

##### Surgical Treatment of Arteriosclerosis

**The Challenge of Arteriosclerosis to Surgeons**  
*Richard L. Varco*, Minneapolis, Minnesota ..... 902

##### Occlusive Arterial Disease—Management by Thromboendarterectomy

*Edwin J. Wylie*, San Francisco, California..... 904

##### Occlusive Arterial Disease—Management by Use of Homografts

*Charles A. Hufnagel*, Washington, D. C..... 912

##### Healing and Fate of Arterial Homografts

*Lester R. Sauvage*, Seattle, Washington..... 916

##### Use of Greater Saphenous Vein Autografts in Reconstruction of Segmental Arterial Occlusions

*Thomas O. Murphy and J. Bradley Aust*, Minneapolis, Minnesota ..... 918

##### Surgical Treatment of Aneurysms of Arteriosclerotic Origin

*Henry T. Bahnson*, Baltimore, Maryland..... 922

##### Plastic Replacement of Diseased Arterial Segments

*Harris B. Shumacker, Jr.*, Indianapolis, Indiana..... 927

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#### GENERAL INFORMATION

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for December, 1955

## MISCELLANEOUS ARTICLES

<b>CURRENT CARDIAC CONCEPTS</b>		<b>IN MEMORIAM</b>	
888	Present Treatment of Subacute Bacterial Endocarditis Wendell H. Hall, M.D., Minneapolis, Minnesota.....	Albert Justus Chesley.....	948
		<b>REPORTS AND ANNOUNCEMENTS</b> .....	950
<b>LABORATORY AIDS</b>		<b>WOMAN'S AUXILIARY</b>	
891	Pathology Has Emerged from the "Deadhouse" George G. Stilwell, M.D., Rochester, Minnesota.....	State Auxiliary Holds Fall Meeting.....	951
		National Auxiliary Holds Conference.....	951
<b>EDITORIALS</b>		<b>MINNESOTA STATE BOARD OF MEDICAL EXAMINERS</b>	
902	Communication: An Overview.....	Minneapolis Midwife Sentenced for False Birth Certificate .....	952
	Tuberculosis Control in the Schools of Minnesota.....		
	The Family Agency and Marital Counselling.....	<b>GENERAL INTEREST</b>	
904	Suburban Medical Migration.....	Personal News .....	953
	A Trend or More?.....	New Locations .....	xxii
		Hospital News .....	xxii
		Minnesota Blue Shield-Blue Cross.....	xxii
<b>PRESIDENT'S LETTER</b>		<b>INDEX TO VOLUME 38</b> .....	955
912	No Time for Littleness.....	<b>BOOK REVIEWS</b> .....	xxiv
		<b>CLASSIFIED ADVERTISING</b> .....	xxxii
918	<b>MEDICAL ECONOMICS</b>	<b>INDEX TO ADVERTISERS</b> .....	xxxiii
	County Society Studies Doctors' Estates.....		
	Medical Costs Survey Notes Trends.....		
	Graduate Medical Education Shows Big Gains.....		
918	Suggestions on Joint Commission on Accreditation Wanted .....		
	Social Security, OASI Figures Noted.....		
921	Folsom Asks More Funds for Medical Research.....		
921	<b>THE DEAN'S PAGE</b>		
927	Minnesota Graduates in Public Health Work.....		

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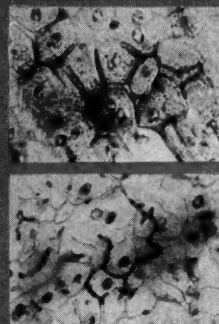
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(1) Clara, M.: *Med. Monatsschr.* 7:356, 1953. (2) Brauer, R. W., and Pessotti, R. L.: *Science* 115:142, 1952. (3) Schwimmer, D.; Boyd, L. J., and Rubin, S. H.: *Bull. New York M. Coll.* 16:102, 1953.



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# *Peripheral and Cerebral Arteriosclerosis*

## **Clinical Aspects of Occlusive Arteriosclerosis of the Extremities**

A. WILBUR DURYEE  
New York, New York

THE physician charged with the management of a patient with arteriosclerosis involving the peripheral vessels is faced with one of the most complex problems in medicine today. All too frequently he is inspired by the glowing claims of pharmaceutical houses, and once having made this diagnosis, he sits down and writes out a prescription for a vasodilating drug, only to be sadly disappointed with the results as the weeks and months roll by. On the other hand, many of us who have had twenty-five years or more experience in this field will often reach a point of frustration as far as therapy is concerned after spending hours in studying an individual problem. However, the last quarter of a century has developed an approach of study which in many cases helps outline a regime of management often producing satisfactory results. Therefore, it is my purpose to look back over the past twenty-five years and try to pick out from the vast amount of information in the literature and from our own personal experiences such findings that will be of value in studying the individual case and in arriving at a proper means of management and outlining such management.

### **Arteriosclerosis**

Kellner has described this disease as an episodic and segmental disease. Its course is bizarre and unpredictable. The broad term "arteriosclerosis" embodies various pathologies of the arterial tree, frequently overlapping each other, but in each individual case one of the forms of the pathology predominates over the others. For example, in the gangrenous ulcers of the skin associated with hypertension, we find the pathology largely limited to the smaller arteries and arteriols supply-

ing the skin. As Allen, Barker and Hines have pointed out, one can roughly subdivide arteriosclerosis into three types. First, there is medial-sclerosis, frequently referred to as Mönckeberg's sclerosis, where most of the pathology involves the medial coat of the artery and where calcinosis is common. The pathological changes associated with this type of lesion rarely involve the intima, and therefore the signs of arterial occlusion are not frequent in this condition. Although usually present in the latter decades of life, calcification of the arteries may occur from infancy on. It may be present for many years without symptoms. However, atheromotosis may complicate the pathology at any time and produce obstructive lesions leading to the production of symptoms of arterial insufficiency.

Atheromotosis or atherosclerosis is the pathological process which brings most of these patients to the physician. Recent observations during the Korean War where careful studies of peripheral vessels were made in young individuals would indicate that changes in the intima may occur in a much earlier age level than previously suspected. It has been thought for years that this disease starts in the fourth and fifth decades of life. However, it is now common knowledge that it is seen very frequently in the second and third decades of life. With advancing years it becomes much more common and probably is most active in the fourth and fifth decades. The intima becomes involved with the development of localized plaques filled with cholesterol and lipid material and associated with thrombotic masses in the lumen of the vessel, either partially or completely occluding its lumen. This pathology is much more frequently found in the larger or medium sized arteries of the extremities than it is in the smaller arteries or arteriols. There

Presented in the Symposium on Arteriosclerosis, University of Minnesota, Minneapolis, September 9, 1955.

is absolutely no set pattern for the development of the lesions which are usually segmental in location and may involve only small areas of one vessel or multiple areas in many vessels. The disease may progress slowly or rapidly and there may be long periods of quiescence.

Involvement of the smaller arteries in an extremity is most frequently associated with hypertensive vascular disease. We have relatively little knowledge as to the early changes in these vessels which are probably largely of a functional nature. As the hypertension persists, organic changes are recognized within these vessels with a tendency for an hypertrophy of the medial coat with secondary thickening of the intima and in some cases complete occlusion of the vessel.

#### Clinical Picture of Peripheral Arteriosclerosis

The patient who presents himself for medical care due to symptoms of occlusive arterial disease in the lower extremities does so because his symptoms are due to some alteration in the blood supply to the tissues in his extremities. The large majority of these individuals are males, most of them beyond the age of forty-five, and over 99 per cent of them have complaints referable to the lower extremities in contrast to the upper extremities. Their presenting symptoms are a result of a combination of factors which tend to reduce the blood supply to the tissues. These factors may be roughly divided into two main groups: the organic changes which have already been discussed, and the associated spastic or functional factors. Before one can approach the problem of therapy, a most careful analysis of each individual case must be carried out in order to determine not only the type of organic change and its location but also the rate of development. A knowledge of the hematological and metabolic picture of the individual must be obtained. Associated anemia or polycythemia or diabetes superimposed on the vascular organic lesions will present other problems in management. In addition, an estimation of the secondary or associated vasospastic state is necessary in the over-all evaluation of the specific case. Various means have been developed to estimate the state of the vasomotor tone. Reflex vasodilatation tests using skin temperature as a guide of such vasodilatation, plethysmographic studies, and in this age of atomic energy radioactive materials and their rate of flow following various methods

of producing vasodilatation may be used to evaluate each case. Even without such detailed studies, one can frequently determine whether vasospasm exists by simple observation of an extremity. Does it become warm and cold alternately? Does it sweat or become dry from one period of observation to another? Are the patient's complaints extremely variable from time to time?

In the early stages of a slowly progressive occlusive disease, this vasomotor state may make up a large element of the clinical picture and account for considerable reduction in blood flow. This is true particularly of the vessels in the skin. At this point it might be well to point out the so-called "borrowing-lending" phenomenon in the lower extremities. It is a well-recognized phenomenon that where vasospasm of the skin occurs, blood supply to the muscles tends to increase; and vice versa, where vasodilatation of the skin vessels is produced by any method, blood supply to the muscles is reduced. It has also been demonstrated that where a muscle is put to use, an opposing resting muscle is temporarily depleted of blood supply. Some of these observations are extremely important in arriving at the proper therapeutic management of these cases.

#### Symptomatology

I shall briefly review the outstanding complaints of a patient with arteriosclerosis of the vessels involving the lower extremities, pointing out their significance:

**Coldness.**—Although coldness may be simply a manifestation of vasospasm and not indicative of organic disease, it is more frequently found in individuals with a rapidly progressing organic disease and an associated vasospastic state. Unilateral coldness is of much more significance than a bilateral coldness from a diagnostic point of view. Coldness which is persistent is of greater significance than coldness which is recurrent. Reduced temperature in digits or in part of an extremity tends to point out localized arterial insufficiency. Often the subjective feeling of coldness is more important than the objective evidence of its existence. Coldness is an indication of changes in skin blood flow but gives one no idea of the blood supply to the muscles of an extremity.

**Paresthesias.**—Many patients in the early stages of occlusive arteriosclerosis will complain

of numbness, tingling and burning. Such symptoms are much more common in those patients suffering from the vascular lesions associated with hypertensive disease than they are with the occlusive process of major vessels due to atherosclerosis. However, when atherosclerosis causes acute occlusion, paresthesias are predominant in the picture. Persistent paresthesias are more indicative of organic blockage while recurrent paresthesias would indicate a picture of recurrent vasospasm alternating with periods of vasodilatation. Again, let me point out that these neurological symptoms are the result of alteration of blood supply to the skin and not to the deeper tissues.

*Intermittent Claudication.*—Here we have a symptom which is directly related to impaired blood supply to muscle. It has nothing to do with the ischemia of skin or subcutaneous tissue. It is a distress frequently described as a tightening, band-like sensation with inability to use an extremity which develops as muscles are inadequately supplied with blood while they are in active use. There is almost immediate relief of this symptom once the muscle is allowed to rest. The symptom returns with the resumption of activity of that muscle. The recurrence of the symptom usually follows almost exactly the same amount of use of the muscle which produced it in the first place. Although some patients will tell you that after the first episode of intermittent claudication their walking distance will increase, it is my personal belief that this increased walking distance is due to the fact that these individuals tend to reduce their speed of walking after the symptom first presents itself and therefore walk a greater distance than they did when the rate of speed was greater.

*Rest Pain.*—This symptom is an indication of serious arterial impairment to the skin and rarely to the subcutaneous and muscular tissues. It indicates that there is insufficient blood to permit adequate nerve nutrition when the patient is at complete rest. It is most frequently observed during the sleeping hours when, with a reduction of blood flow due to a slow cardiac function, pain develops which awakens the patient from a sound sleep. With dependency of an extremity and perhaps a little physical activity to raise the blood pressure and pulse rate, there is temporary relief of the pain.

*Weakness.*—The complaint of weakness is one which usually develops after the disease has been present for a long period of time and muscle blood supply has been reduced to a point where atrophy takes place. It also occurs after a long period of disuse with atrophy and with associated osteoporosis.

### Objective Findings

*Trophic Changes.*—On inspection of an extremity with arterial insufficiency due to arteriosclerosis, one frequently notes trophic changes in the skin, reduction in hair growth, transverse ridging of the nails, and actual muscle atrophy. These observations are indicative not only of occlusive arterial disease but may occur in all trophic and functional vascular pathology. However, they are more common where occlusive organic disease is present.

*Color Changes.*—The classical rubor on dependency and pallor on elevation are almost diagnostic of arterial occlusive disease. With arterial insufficiency to the skin, one has a delayed hyperaemia after blood has been expressed from a local capillary bed. In acute occlusion mottling and cyanosis and marbling of the skin may occur.

*Temperature Changes.*—Objectively as well as subjectively, one can note by palpation areas of decreased temperature associated with arterial insufficiency. It might be well to point out that frequently the level of occlusion in a main arterial supply is much higher than the temperature level change. In other words, an occlusion in the lower femoral artery frequently is manifested by a coldness extending from the mid-calf area downward. The sudden development of warmth in an extremity which was previously cold, particularly if it is a localized area of warmth, is very suggestive of secondary infection.

*Determination of Vessel Pulsation.*—This can usually be determined by simple palpation over the major vessels of the extremities, such as the femoral, popliteal, posterior tibial and the dorsalis pedis arteries. However, such a method of testing is unsatisfactory in certain individuals because of associated edema, mal-position of vessels, or obesity. In such individuals, the use of an oscilometer will frequently determine whether or not a pulsation is present. This instrument is not one of precision and should not be used to determine

## ARTERIOSCLEROSIS OF THE EXTREMITIES—DURYEE

accurately minor changes between extremities or in the same extremity from time to time. However, it is of a great deal of assistance in determining whether there are gross changes and whether or not pulses are present. Examination for pulsations must be carried out in a warm environment with the patient relaxed. There are certain individuals in whom coldness or emotion will cause vasospasm of major vessels. In rare instances examination must be carried out following a paravertebral block or some other method of producing vasodilatation.

**Gangrene and Ulceration.**—In occlusive arterial disease due to arteriosclerosis, gangrene is almost universally a distal affair, occurring either in the toes or the heel and progressing proximally from these locations. In rare instances infarction of the skin may occur in any part of the extremity, usually in the leg and not in the thigh. Such lesions are extremely painful and are frequently multiple.

The development of gangrene usually depends on the rapidity of the development of the occlusive process, being much more frequent in the acute occlusion than in the chronic one because of the inability of collateral circulation to develop to replace the occluded main vessels. Ulceration of the skin in the lower legs, particularly laterally, may indicate a form of gangrene of the skin secondary to hypertensive disease with secondary changes in the arterioles and smaller arteries, the so-called hypertensive ulcers.

**Edema.**—Edema as the direct result of arterial occlusion does not occur. Indirectly it may occur on two bases—either secondary to venous or lymphatic occlusion as the result of impaired arterial supply and thrombosis or infection, or as the result of atony of the tissues and dependency of the extremities. In advanced arteriosclerotic disease of the extremities, many patients sit for hours with their feet in a dependent position in order to obtain some relief from the pain. Edema is common in these individuals.

### Laboratory

**Blood Studies.**—As indicated previously, an accurate blood count including a hematocrit study is important to rule out abnormal concentrations or dilutions of the blood as well as to rule out other blood dyscrasias such as the leukemias.

Prothrombin time studies are necessary where anticoagulants are to be used therapeutically. Otherwise they have no value. The estimation of the vitamin C level in the blood should be done in all cases, as many of these individuals have a poor intake of this vitamin with a tendency for increased capillary bleeding which in turn tends to complicate the skin lesions of the lower extremities. Blood sugar and blood lipid determinations should be done on all patients. Associated diabetes should be ruled out. Until we know more about the relationship of lipid metabolism to this disease, the acquisition of this information may not be of too much value. However, because of the close relationship of abnormal lipid metabolism to atherosclerosis, each case should have a careful work-up of this type because in the future it may be of real value.

**X-ray Studies.**—Determination of calcification of vessels should be carried out in each case. This information is of no value in estimating the functional capacity of the vessels but does give one evidence of abnormal pathology in the wall of the vessel. X-rays are also helpful in determining blood supply to bone and indirectly measuring blood supply by determining the amount of osteoporosis present.

Visualization of the luminae of the arteries and collateral circulation by the injection of contrast media is a most important diagnostic procedure in these cases of occlusive disease. Since we now recognize the segmental distribution of many of these occlusive lesions, it is important to localize such areas if they are to be attacked from the surgical standpoint. I am sure that my successor on this program will point out the value of such a diagnostic procedure in studying the lesions of the terminal aorta. Such tests are equally important in studying the blood flow particularly through the femoral artery. Moreover, in those cases of arteriosclerosis complicated by aneurysms, such lesions may be readily picked up by this method.

**Measurement of Cardiac Function.**—Since the blood flow through the peripheral circulation is dependent on satisfactory cardiac function, it is necessary to carry out routine studies to determine the function of the heart in every patient. An electrocardiogram and fluoroscopic and clinical study of the heart action should be routine.

### Management of Arteriosclerotic Peripheral Vascular Disease

I prefer the term "management" of arteriosclerotic peripheral vascular disease to the term "treatment" of arteriosclerotic peripheral vascular disease. We have no specific therapy for arteriosclerosis and at best we can only tend to direct or guide its course and to control the complications which arise. There are certain basic principles of management which we shall discuss. They are as follows:

1. To increase collateral circulation at a rate greater than the occlusive process develops.
2. To overcome vasospasm.
3. To prevent and to control infection.
4. To prevent and to control thrombosis.
5. To remove local areas of arterial obstruction.
6. To treat associated disease.

We shall discuss each of these approaches in detail.

*To Increase Collateral Circulation.*—In those cases where the predominant symptoms point to poor blood supply to muscle and where segmental blockage cannot be removed, I know of only one procedure which may help develop collateral circulation to the important muscles of a lower extremity. That is the proper use of these muscles. In a series of over a hundred cases treated privately and in our vascular clinic, we have followed a group of individuals with intermittent claudication as the only symptom and have limited their treatment largely to simple advice as to the use of their extremities. Considerable time has been spent with them from visit to visit, detailing an outline of physical activity where the leg muscles are used routinely but well within their tolerance for activity. In other words, these individuals are urged to walk frequently short distances but never under any circumstances to force their walking against any distress in the legs. As this paper was prepared, a rough review of these cases would indicate that over 75 per cent of them had increased walking distance at the end of a year and less than 3 per cent of them had serious complications of their pathology with loss of digits or in one case an extremity. At the end of three years, over 60 per cent still had increased walking distance and only 6 per cent had developed serious complications.

*Overcoming Vasospasm or the Production of Vasodilatation.*—In those individuals where collateral circulation to the skin must be developed, our second principle of management is applicable, and that is the overcoming of vasospasm. In this group of individuals, the complete abstinence from smoking is extremely important since tobacco causes a high degree of spasm of the skin blood vessels, particularly in the digits; and where such vasospastic ability is still present, the continued use of tobacco interferes with the development of collateral circulation and cuts down the available blood supply. This holds true for any other vasospastic drug such as ergot. Exposure to extremes of temperature should be eliminated. Emotional factors should be controlled as far as possible.

Many physicians have been sadly led astray by the claims of the commercial houses and by certain papers in the literature advocating vasodilating drug therapy. The use of so-called oral vasodilators or the use of these same substances parenterally or intravenously is contra-indicated in practically all cases of peripheral arteriosclerosis. Certainly in those individuals with intermittent claudication as the main symptom the use of these drugs does not increase the blood flow to the muscle. If they do increase blood flow to the skin they probably do so to the healthier parts of the body and to the skin over the healthier extremities rather than to those with impaired blood supply. Purely from a long-term observation of the use of these drugs in our clinic, I have been impressed with their failure to produce results when given as described above. Many of the vasodilating drugs have been put on the market following a short period of experimental use on animals or on normal humans. When applied to our problem which we are discussing today, they are often without value and occasionally detrimental. If one reads the literature supplied with these preparations and has some basic knowledge of the diseases for which they are being prescribed, one cannot help but be impressed by the fallacy of their application. For example, one of the newer drugs which has recently reached the market is claimed to have no effect on increasing skin circulation but marked effect on increasing muscle circulation. Literature from abroad is supplied with this drug by the contact man indicating that in normal human beings the blood supply to the muscle is markedly increased. Yet when this drug

is given a clinical trial, there is no indication that it relieves symptoms of claudication. Moreover, in the advertising it is claimed to be an excellent drug for the treatment of a Raynaud's syndrome. In other words, the manufacturers contradict themselves in stating that it is not a skin vasodilator in one breath and then claiming that it will help Raynaud's disease which is a disease of vasospasm of the blood vessels to the skin. This particular drug has already received much publicity in many lay journals.

If vasodilating drugs are to be used, they should be directed toward the nerve control of the blood vessels in the involved extremity. There is some evidence that if they are injected intra-arterially, local vasodilatation can be achieved. However, in our own experience, this vasodilatation may occur to a maximal degree proximally in the skin of the involved extremity while the distal parts, where the need for vasodilatation is greatest, are robbed of blood. Therefore, the most logical method of increasing skin blood flow is by the elimination of vasospasm by the blocking of the sympathetic nerve supply or by its severance with a surgical sympathectomy. In those individuals with impaired skin blood supply to a point where serious complications of ulceration and gangrene may develop, sympathectomy is indicated. Moreover, it is my belief that sympathectomy does not increase blood supply to the muscles and is contra-indicated in the management of intermittent claudication. We have seen numerous examples of further reduction in walking distance following lumbar sympathectomy with a most satisfactory increase of blood supply to the skin. Relaxation of the entire nervous system with the use of sedatives and the so-called tranquilizing drugs and with alcohol sometimes seems to help increase skin circulation.

*Control of Infection.*—I am sure that most clinics can report a reduction in amputation rate in peripheral arteriosclerosis since the advent of the antibiotics. Certainly every individual with advanced arteriosclerosis should have everything done prophylactically to prevent infection and to treat it once it occurs. This means the elimination of all fungus invasion of the skin by bland fungicide therapy and the immediate treatment of any wound or infected area with systemic antibiotics. Because of the reduced blood supply to the tissues, adequate dosage is indicated to get the

local concentration at a satisfactory level to combat the infection. The use of local antibiotics in this condition is of relatively little value, although small areas of ulceration may be partially cleared with some of the local preparations.

*Prevention of Thrombosis.*—One immediately thinks of the use of anticoagulants when one mentions thrombosis. However, clotting in the diseased arteries can be delayed or prevented by other methods than with the use of anticoagulants. By maintaining a good body metabolism which increases the rate of blood flow, by maintaining hydration and preventing hemoconcentration, and by preventing the slowing down of blood through vasospasm in the collaterals, thrombosis may frequently be avoided. I do not believe that we have reached a point where every patient with peripheral arteriosclerosis should be given anticoagulants prophylactically. The dangers of hemorrhage are ever present and particularly with the possibility of cerebral vascular accidents in the hypertensive group, there is no indication for their routine use. However, in the acute arterial occlusion, immediate anticoagulant therapy with the rapid-acting Heparin is indicated and perhaps later the use of the slower-acting drugs to prevent the complication of an ascending thrombosis or an associated venous thrombosis. This is particularly true if the patient has to be put to bed at rest. These anticoagulants should be continued until vasospasm can be overcome and until the patient again becomes ambulatory or amputation has taken place.

*Remove Local Areas of Obstruction.*—I shall leave it to others on this program to discuss the surgical management of occlusive arterial disease of an arteriosclerotic nature, but we are all familiar with the excellent results obtained by segmental grafting or the use of by-pass shunts, or even in some cases of endarterectomy. Many patients have been given a marked return of function of the lower extremities and relief of rest pain by such surgical procedures. However, since this disease is a progressive one, unfortunately the use of arterial grafts is probably only a temporary measure. In some patients with long periods of remission, their value may be great. In others, secondary thrombosis shortly after the surgery or involvement of other main arterial trunks may make this procedure of little value. It

will be several years before we shall be able to arrive at any correct evaluation of this therapy.

*Treatment of Associated Disease.*—As in all fields of medicine, the most satisfactory results are obtained when all factors in a given case are managed to the best of the physician's ability. Certainly diabetes in a patient with arteriosclerosis needs careful management to avoid some of the serious complications of this disease when it is out of control. Although many authors have stated that the incidence of gangrene is no greater in the diabetic than in the non-diabetic, it is my personal opinion from clinical observation that it is far greater in the diabetic. Even in those diabetics where control seems to be satisfactory for a number of years, the underlying arteriosclerosis seems to be a more major pathology than it is in the non-diabetic.

The treatment of any associated cardiac pathology is of utmost importance because satisfactory blood supply may not be obtained if cardiac function is not normal. This is especially true if there has been an acute cardiac episode complicating the management of peripheral problems or in those individuals where increasing exercise is wise in the management of the peripheral circulation. Many of our patients are handicapped because of the fact that coronary insufficiency limits the individual with intermittent claudication who should increase his walking but who has to diminish his walking because of the heart vessel involvement. Weight reduction is most important as the individual who is obese tends to have a more rapidly progressing arteriosclerosis.

He also is greatly handicapped because of reduced activity since his legs with impaired blood supply will not carry excessive weight. Finally, these patients must be told to live within their capacities, and a careful consultation with them from this standpoint is important. If they understand their disease, its variability, and the need for relaxation, much will be gained in the management of the entire problem.

### Summary

There have been many angles that I have not had sufficient time to discuss. The use of various mechanical apparatus to increase circulation has not been covered. These machines have found a diminishing use in the management of this disease. The entire question of posture to blood flow in the extremities so carefully investigated by Wilkins has not been reviewed. It should be emphasized again that each individual case should be carefully studied and that combined approaches to therapy should be used to obtain the maximal blood flow. Careful co-operation between the medical man and the surgeon with the patient treated as a complete individual, and not the extremity alone, will produce a most satisfactory outcome. Surgery will play a more important part in the management of peripheral arteriosclerosis than it has in the past. Drugs will play a lesser role. Nature in many instances will repair damage by the development of collateral circulation despite the aid of the doctor. Too often he takes or is given credit when the natural reparative processes of the body are responsible.

### Discussion

DAVITT A. FELDER, St. Paul, Minnesota: In the drama of the remarkable and rapid advances being made in the treatment of arteriosclerotic problems today, one may easily lose sight of certain essential points characteristic of this disease. Because of the sometime brilliant results of his accomplishments the surgeon may more often lose sight of the over-all picture of the patient than others. But we all might do well to consider the statement of the vascular surgeon Haimovici, who said, "Critical evaluation of any type of treatment must obviously be made against the background of the natural course of the disease."<sup>\*</sup>

It seems illogical to subject a patient to the surgical hazard and discomfort incident to the removal of an asymptomatic aortic aneurysm only to have him die then or soon afterwards of a coronary or cerebral ictus.

There are apparently some less obvious possible pit-

falls than this in the treatment of arteriosclerosis that present themselves. I am sure that most of us in this audience have pondered the question of the effect of general vasodilatation on an ischemic arteriosclerotic extremity. Yet we use vasodilating agents daily. It is likely that the drop in blood pressure induced by these drugs plus the reduction in the amount of blood in a sclerotic segment of the periphery might be responsible for thromboses in these areas.

We have shown consistently in our laboratory<sup>\*\*</sup> in a controlled environment that the extremity with sclerotic

(Continued on Page 870)

<sup>\*</sup>Haimovici, H.: Peripheral arterial embolism. *Angiology*, 1:20-45, 1950.

<sup>\*\*</sup>Surgical Research Laboratory, St. Joseph's Hospital, St. Paul, Minnesota.

# Clinical Aspects of Arteriosclerotic Aneurysm and Arteriosclerotic Occlusion of the Abdominal Aorta

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## Aneurysm of the Abdominal Aorta

SINCE aneurysms of the abdominal aorta are not rare, physicians in this country may expect to encounter them even more often in medical practice in the future inasmuch as the average age of our population is increasing steadily.

The cause is almost always arteriosclerosis. Mills and Horton<sup>1</sup> found that 86 per cent of their series of patients with aneurysm of the abdominal aorta were more than fifty years of age and that twice as many men were affected as women.

The prognosis is poor for patients who do not have treatment. Patients who have been treated surgically have not been followed long enough so that the effect of such treatment on the long-term prognosis is known, but it is known that surgical treatment may be a lifesaving measure for some patients and that many patients have been relieved of symptoms and have lived for many months longer than they could have lived without such treatment.

In Estes<sup>2</sup> series of 102 patients, of whom ninety-seven had aneurysms attributed to arteriosclerosis, a third of ninety-one traced patients died within a year following diagnosis, half of sixty-three traced patients died within three years and about three-fourths of forty-six traced patients died within five years. Of the patients who died, 63 per cent died from rupture of the aneurysm and 37 per cent from other causes. The severity of symptoms apparently had little relationship to the eventual prognosis as those who had no symptoms at the time the diagnosis was made lived no longer than those who had symptoms due to the aneurysm. This may not be a

significant observation, however, as a larger relative number of patients with symptoms would consult a physician, and, therefore, would have been included in Estes<sup>2</sup> study than those who had no symptoms.

Estes<sup>2</sup> compared the survival of his group with the life expectancy of the "normal" population of the same average age. He found that whereas 35 per cent of a "normal" population which is sixty-five years of age will die within eight years, 90 per cent of his group would die within this same period. The important question is how many patients would have died from complications of the aneurysm that might have been prevented or have been delayed by methods of treatment available today. From a survey of Estes' findings it appears that almost two thirds of the patients known to be dead died from complications of the aneurysm, usually a rupture, within the eight years after diagnosis. This complication presumably might have been avoided by surgical treatment if it had been available. This does not mean, however, that the life expectancy of these patients may not have been shortened anyway by other complications of their disseminated atherosclerotic vascular disease.

Abdominal pain and the presence of an abdominal mass noted by the patient are the two symptoms of aneurysm of the abdominal aorta most frequently encountered. The pain may be persistent or intermittent. Severe, persistent pain may be present even when there has been no rupture and is due probably to a periaortic inflammatory type of reaction sometimes found in patients with abdominal aortic aneurysms. The pain of abdominal aortic aneurysm commonly is a diffuse type of distress in the middle and lower portion of the abdomen or in the lower part of the back. There is a tendency for the pain to be more prominent on the left and to extend down the left side of the abdomen. Sometimes the pain is equally distributed on both sides of

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the abdomen and back with extension into both groins and anterior regions of the thighs.

The one common physical sign is an expansile, pulsatile mass in the abdomen. The bulk of the mass is located usually in the left side of the abdomen. The diagnosis of an aneurysm should not be made solely on the basis of this physical finding unless the mass can be grasped by deep pressure with both hands and localized bilateral, expanding pulsation can be felt. Nervous patients frequently complain of abdominal throbbing and pulsation and in such patients a prominent pulsation may be felt in an aorta of normal size. Patients who have lordotic spinal columns or elderly persons with sclerotic, tortuous aortas may have palpable abdominal pulsations which simulate the pulsations in an aneurysm. A thrill or bruit is present over an aneurysm in only about half of the patients and its presence or absence does not help much in the diagnosis.

It is significant that a third of the patients in Estes<sup>2</sup> group had no symptoms referable to the aneurysm at the time of examination. The aneurysms of these patients were discovered either on routine physical examination or incidentally by x-ray examination or surgical exploration carried out because of other complaints presented by the patient. This emphasizes the value of careful palpation of the abdominal aorta in the course of the physical examination of all older patients.

Often the aneurysmal sac is partially or almost completely filled with old and new blood clots, and these may affect the degree of pulsation which can be felt as well as the finding on roentgenographic examination. Occasionally the renal artery may be included in the aneurysmal sac, and the blood flow through the renal artery may be impeded by the blood clot in the aneurysm or by the atheromatous plaques. I have observed two patients in whom this type of involvement of the renal artery apparently caused moderately severe hypertension. The most common serious complication is leaking or rupture of the aneurysm. Erosion of the vertebra and pressure on neighboring nerve trunks or organs are rare occurrences.

The diagnosis is not difficult and usually can be made on the basis of the findings on physical examination. A plain roentgenogram of the abdomen will usually show evidence of a soft tissue mass, calcified plaques or in some cases a cur-

vilinear area of calcification which is characteristic of an aneurysm of the abdominal aorta. Aortography is not essential for diagnosis although it is helpful in the evaluation of treatment. The aortogram will give information of importance concerning the relationship of arterial trunks (particularly the renal and mesenteric arteries) to the aneurysm and the patency of these arteries. The presence and size of an intraluminal blood clot is usually well demonstrated in the aortogram. These blood clots may give a misleading picture in that they may almost entirely fill even a very large aneurysm and may cause the lumen to appear normal or nearly normal in size in the aortogram. In such a situation the location of the walls of the aneurysm may be apparent from the curvilinear area of calcification in the wall previously mentioned as being shown in the roentgenogram. This area may be several inches away from the lumen as demonstrated in the aortogram. Occasionally when physical examination and roentgenographic findings are inconclusive, abdominal exploration may be necessary to confirm or disprove the diagnosis.

#### Occlusion of the Abdominal Aorta

Although the symptom of high intermittent claudication with distress in the lower part of the back, hips and thighs on walking has been recognized for many years, only in recent years has it been realized that this syndrome was often due to a segmental occlusion of the abdominal aorta. Occlusion of the abdominal aorta is almost always a form of arteriosclerosis obliterans and except for its location in the abdominal aorta is essentially the same process that occurs in the arteriosclerotic disease affecting the arteries of the lower extremities, designated for many years as "arteriosclerosis obliterans." Rarely, simple thrombosis alone may cause occlusion of the abdominal aorta but almost always when thrombosis is present, the occlusion is due to a thrombus superimposed on one or more atheromatous plaques. Occasionally the abdominal aorta may be partially or functionally completely occluded by atheromata alone. The occlusion may involve the renal and mesenteric arteries and in some instances of this type complications such as hypertension or infarction of the bowel may result and eventually may cause the death of the patient.

Frequently periaortitis is present and causes adhesions to the vena cava and other structures in the region.

The disease is usually progressive over a period of five to ten years. Although men are affected more commonly than women, occlusive atherosclerosis in this location is the only form of arteriosclerosis that I know of that not infrequently causes symptoms in their early forties in women who do not have diabetes. Arteriosclerosis obliterans which involves the lower extremities almost never occurs in women, even in those with diabetes, before the age of fifty years or in women without diabetes before the age of sixty years. There is something unique and intriguing, especially as to the cause of arteriosclerosis, about this small group of young women without diabetes who have segmental atheromatous occlusion of the abdominal aorta.

Four points should be kept in mind in the clinical evaluation of a patient with occlusion of the abdominal aorta, especially when treatment is being considered: (1) Most of these patients have disseminated atherosclerosis, and complications from coronary or cerebral arterial occlusion are not unusual. (2) Segmental occlusion of the abdominal aorta alone does not often result in severe ischemia in the feet and legs, and ischemic ulcer or gangrene are infrequent complications, at least during the early years of the disease. (3) In addition to the occlusion in the aorta, segments of the arteries distal to the aorta such as the femoral or popliteal arteries may be occluded also by atheromata and thrombi. (4) Enough knowledge of the natural history of this condition has not yet been acquired so that any satisfactory conclusion can be reached as to the eventual incidence of loss of life or of limb from complications of the disease or of the life expectancy of patients who have occlusion of the abdominal aorta.

Chronic occlusion of the abdominal aorta is characterized symptomatically by the gradual development of fatigue and pain in the back, hips and thighs which at first occurs only on prolonged exercise and is relieved by standing. Occasionally in proved occlusion of the lower abdominal aorta or iliac arteries the distress of intermittent claudication may be confined to the calves of the legs. Later in the course of the disease the distance that can be walked without distress is lessened and in many instances may be reduced to less than one block. Some patients may complain of a vague distress and fatigue low in the back and in the hips on prolonged

standing or even at rest. Usually this type of static distress is not considered to be due to arterial insufficiency but two patients have been largely relieved of this type of distress following successful removal of the occluded portion of the aorta and re-establishment of blood flow. I have seen two women who complained of distress low in the back, and in the hips and thighs while making beds. This was largely relieved by surgical treatment of an occluded abdominal aorta. Recently also I have had a man, a widower, who had to make up his own bed; he, too, had noted this type of distress, at least to a sufficient degree that he felt justified in getting someone else to make his bed. Dr. Ellis has recently operated on the abdominal aorta of this patient successfully but the patient has not as yet had an opportunity to try out his bed-making ability. Coldness and pallor of the lower extremities are unusual complaints. Inability to have and to maintain an erection of the penis may occur; this apparently is due to an insufficient supply of blood to that organ.

Careful palpation will disclose that pulsations are diminished or absent in the lower part of the abdominal aorta and below the bifurcation of the aorta. It is well to bear in mind that as in coarctation of the aorta occasionally pulses in the femoral arteries may be surprisingly good, although not normal, even when there is complete or almost complete segmental occlusion of the abdominal aorta. Examination may reveal varying degrees of coldness of the feet and legs and some pallor of the feet on elevation of the lower extremities. These changes are usually not marked unless the abdominal aorta is occluded extensively or unless the arteries are occluded below the bifurcation of the aorta. A systolic murmur may be heard over the lower part of the abdomen and in some cases in the back over the lumbar region.

Laboratory findings and plain roentgenograms are of little aid in the diagnosis of occlusion of the abdominal aorta although a roentgenogram of the region of the abdominal aorta may reveal varying degrees of calcification of the aorta. An aortogram usually will reveal the site and degree of the obstruction of the aorta and may reveal additional areas of obstruction in the iliac and upper portions of the femoral arteries if they

(Continued on Page 879)

# Clinical Picture of Cerebral Arteriosclerosis

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WHEN the term arteriosclerosis is used in its broadest sense to include all of the abnormal processes which involve arteries, a rather large number of pathological conditions affecting the arteries of the brain can be classified under the regional caption, cerebral arteriosclerosis (Table I). Of course, all of these are by no means equally represented in the field of clinical medicine, and indeed the great majority of human illnesses which prove to be due to diseases of the cerebral arteries are the result of but one of the conditions listed, namely, atherosclerosis. The following remarks will, therefore, pertain for the most part to cerebral atherosclerosis, but before proceeding to the main topic, brief reference will be made to some of the other pathological processes included in the above list. While a few of these are more or less specific for brain vessels (ferruginization, capillary sclerosis, saccular aneurysmal dilatation, et cetera), many also involve arteries elsewhere in the body (hypertensive hypertrophy, medial hyalinization, arterial necrosis, Mönckeberg's medial sclerosis, Erdheim's cystic medionecrosis, the arteritides, "Buerger's disease," et cetera).

Hypertensive medial hypertrophy, judging from routine clinico-pathologic studies, does not compromise cerebral blood flow, the narrowing of the arterial lumen apparently being offset by the increase in the head of arterial pressure. Hyalinization of the media likewise does not influence blood flow. Arterial necrosis and fibrin impregnation are seen only in the most aggravated stage of severe advancing hypertension, and are but part of the pathological picture underlying what the clinician refers to as acute hypertensive encephalopathy. The vascular abnormality which results in primary intracerebral hemorrhage is no clearer to us now than it was 100 years ago. Using postmortem neoprene injections into the middle cerebral artery in whose territory a hem-

TABLE I. DISEASES OF THE CEREBRAL ARTERIES

1. Atherosclerosis.
2. Changes associated with arterial hypertension.
  - (a) Medial hypertrophy.
  - (b) Hyalinization of media in hypertension of long duration.
  - (c) Arterial necrosis and fibrin impregnation of severe hypertension.
  - (d) Vascular alteration underlying primary intracerebral hemorrhage.
3. Aging or "wear and tear."
4. "Thromboangiitis obliterans."
5. The arteritides—Polyarteritis nodosa.
  - Temporal "giant cell" arteritis.
  - Carotid "giant-cell" arteritis.
  - Non-infectious granulomatous arteritis.
  - Arteritis associated with meningitis—syphilitic, tuberculous, influenza, et cetera.
  - Rheumatic arteritis.
  - Lupus erythematosus.
  - Septic embolism.
  - Unclassified arteritis.
6. Abnormalities underlying and accompanying the formation of saccular, fusiform, globular, and diffuse aneurysms.
7. Ferruginization of cerebral arteries.
8. Calcific deposition in internal carotid arteries within the cavernous sinus.
9. Thrombotic acroangiothrombosis.
10. Mönckeberg's medial arteriosclerosis.
11. Cystic medionecrosis of Erdheim.
12. Capillary sclerosis.
13. Radiation arteriopathy.
14. Post-migrainous edema.

orrhage has arisen, it has been possible in several cases to find in the lenticulo-striate group of vessels a single ruptured artery which probably represented the bleeding point. However, the underlying vascular disease has not been studied as yet. The arterial changes which occur in normotensives with increasing age, including redundancy, enlargement, slight thickening, and increased opacity of the wall, splitting and fraying of the elastica, et cetera, have not been shown to lead to any recognizable symptomatology or to any pathological alterations in cerebral tissues. Mönckeberg's medial sclerosis is not seen in the cerebral vessels distal to the circle of Willis, but has been reported in the carotid artery within the

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cavernous sinus, where it probably never causes any circulatory disturbance. Erdheim's cystic medionecrosis at times involves the common carotid artery, and occasionally an aneurysmal dissection starting in the aorta extends upwards as far as the carotid sinus, resulting in carotid occlusion. The cerebral arteritides unfortunately must be completely omitted from this discussion because of the restrictions of time. Ferruginization of the capillaries and small intracerebral arteries is usually an incidental finding and is encountered in approximately 60 per cent of the brains removed at routine autopsy. Even though the vessels of the basal ganglia, at times become severely involved, extrapyramidal signs and symptoms seem never to arise.

Capillary sclerosis, in which a fine network of reticulin can be demonstrated around the smaller cerebral vessels by the use of silver stains, has in the past been held responsible for senile mental deterioration, the contention being that the connective tissue proliferation hampers a free exchange of nutriment between the vessels and the surrounding parenchymal elements. Gellerstedt, however, found no relationship between aging, mental change, and capillary sclerosis. Cerebral thromboangiitis obliterans, or the alteration of brain tissues classed under that term, is an important subject and will be briefly discussed later.

Turning now to the main theme, atherosclerosis, I think it can be agreed that for the most part cerebral atherosclerosis produces symptoms and signs by only one mechanism, namely, cerebral ischemia due to narrowing or occlusion of one or more cerebral arteries. The atherosclerotic plaque itself is probably asymptomatic, although hemorrhages into a plaque could conceivably lead to headache of a vascular type. Headache is a frequent accompaniment of cerebral thrombosis. Atherosclerosis is commonly held to be the cause of some of the fusiform and diffuse aneurysms of the basilar and carotid arteries. These aneurysms may give rise to symptoms via pressure on neighboring structures, and in this respect the clinical picture might be considered a special manifestation of atherosclerosis. However, there should be much skepticism concerning the rôle of atherosclerosis in these aneurysms for the same dilatations are seen in the absence or near absence of atherosclerosis. It is not improbable that the physical factors which influence the formation

of atherosclerosis often lead to its early appearance in the walls of these aneurysms, and thus the deposition of atherosclerosis could be regarded as secondary, not primary.

Atherosclerosis has often been reported to be either a direct cause or at least a contributory cause of hypertensive intracerebral hemorrhage. There is, as yet, no substantial evidence that it plays any significant part. Indeed it is a fact that the actual site of hypertensive bleeding has never been identified microscopically, and therefore it must follow that it would be impossible with any certainty to link intracerebral hemorrhage to the presence of atherosclerosis. At times hemorrhage takes place when visible atherosclerosis is entirely lacking in the cerebral arteries, and on the other hand cerebral atherosclerosis may be most advanced and hemorrhage fail to occur. This negative evidence is of course only indirect and further study of the problem is required. Occasionally, acute subarachnoid hemorrhage is attributed to "rupture of a plaque of atherosclerosis" on one of the major cerebral arteries. This event has never been encountered personally in the neuropathological examination of many cases of vascular disease, and it must occur only rarely, if at all.

Atherosclerosis has also been reported to play a part both in the formation of saccular aneurysms and in their rupture, but this is quite unlikely since in many cases there is no sign whatsoever of atherosclerotic deposition. Not infrequently a plaque of atherosclerosis is found in the cap of a saccular aneurysm when the nearby cerebral arteries show none at all and this is suggestive evidence that special local factors probably physical lead secondarily to deposits of atheroma in the wall of the aneurysm rather than that atherosclerosis primarily causes the formation of an aneurysm. It is of interest that the occurrence of a plaque within a saccular aneurysm provides an opportunity to study an atheroma as it evolves in the subintima of an artery uninfluenced by the elastic lamina and the muscular media, since both of these are absent from the aneurysmal wall.

The few conditions just mentioned in which atherosclerosis is suspected of being a factor but has not yet been proved to play a causative rôle comprise the chief exceptions to the statement made earlier, namely, that cerebral atherosclerosis in most instances produces neurological illness

only in so far as it creates cerebral ischemia.

In order to better understand the clinical consequences of cerebral atherosclerosis it is desirable first to examine some of the characteristics of atherosclerosis as they are portrayed at pathological examination. A brief review of its incidence, distribution, severity, secondary changes, et cetera, although knowledge of these is still imperfect, will provide the groundwork for a more thorough appreciation of the clinical picture.

Qualitatively atherosclerosis of the cerebral arteries is approximately the same as the process elsewhere in the body and differs only in minor respects, for example, atheromatous ulceration is infrequent. Its severity in cerebral vessels roughly parallels that of other organs of the body, aorta, heart, and limbs, but in most instances is somewhat less advanced, occasionally more so. Therefore, in the majority of cases in which atherosclerosis has produced cerebral disease, there will be evidence of atherosclerosis elsewhere, for example, angina pectoris, myocardial infarction, electrocardiographic abnormalities, absent pulsation in one or more vessels of the lower limbs, crural intermittent claudication and occasionally subclavian obstruction. It is wrong to emphasize that there are marked differences in the severity of atherosclerosis in cerebral vessels and vessels in other parts.

There are sites of predilection for the deposition of atherosclerosis within the cerebral arterial tree. In keeping with the influence of physical factors in the formation of atherosclerosis, the regions of predilection are for the most part at bifurcations, branchings, and curves. Figure 1 illustrates diagrammatically this pattern which must be considered as only a general guide and not a hard and fast formula. The carotid and basilar systems are approximately equally affected although cases will be encountered in which one shows much more atherosclerosis than the other. In general, the large arteries at the base of the brain are the first and most severely involved, the smaller surface vessels often being spared, especially when the blood pressure is normal. The special sites of atherosclerotic deposition are as follows: Within the carotid sinus in the neck, in the carotid siphon extending from the origin of the ophthalmic artery distally to the region of the origin of the anterior cerebral artery, at the first major bifurcation of the middle cerebral artery, in the anterior cerebral artery as it curves

posteriorly over the genu of the corpus callosum; in the vertebral artery as it penetrates the dura, in the vertebrals where they join to form the basilar artery, in the basilar artery 5 to 10 mm.

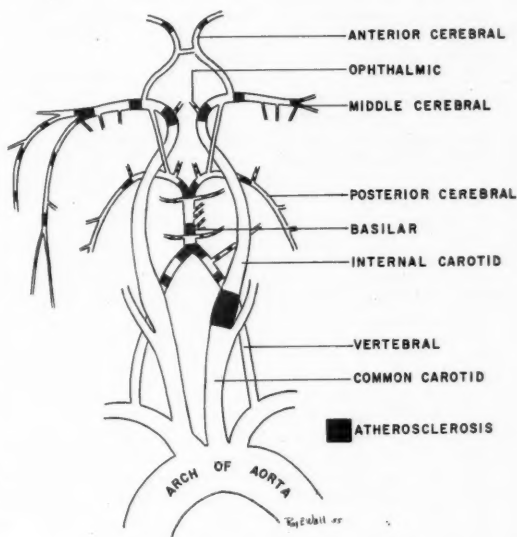


Fig. 1. Diagram of the chief sites of atherosclerotic deposition in the cerebral arteries. The tendency to localize at bifurcations, branchings, and curves is striking.

above its origin, and in the region of its upper bifurcation often involving the proximal portion of the posterior cerebral arteries, and in the posterior cerebral arteries as they curve posteriorly round the cerebral peduncles. The intervening regions of these arteries also will often show deposits of atherosclerosis, but the above sites usually are earlier and more severely involved and are therefore the places at which thrombosis will most likely occur. These regions of predilection exist in the presence of both normal and high blood pressure, but hypertension in addition clearly influences the atherosclerotic process in at least three ways: (1) in general, the process is aggravated, appearing at an earlier age and being more severe; (2) the deposition is more uniform along the vessel either producing a tree bark effect or a dense yellow coating; (3) of greatest significance, however, is the effect of hypertension in leading to the deposition of atherosclerosis in the smaller arteries on the surface of the cerebral hemispheres and over the cerebellum, as well as in the small penetrating arteries which arise from the internal carotid,

## CEREBRAL ARTERIOSCLEROSIS—FISHER

TABLE II. FACTORS WHICH DETERMINE THE OCCURRENCE AND SEVERITY OF CEREBRAL ISCHEMIA IN CEREBRAL ATHEROSCLEROSIS

1. *The degree of narrowing of the arterial lumen*—the size of the plaque, the occurrence of superimposed thrombosis, the speed of thrombosis, and its extension; hemorrhage into the plaque, edema of the plaque—cerebral embolism.
2. *The availability of collateral blood flow*—the circle of Willis, the meningeal anastomatic channels, the external carotid artery.
3. *The maintenance of the intracranial arterial pressure and the intracranial blood flow*—the great importance of the systemic blood pressure—the influence of postural changes, sleep, oversedation, and hypotensive drugs. Carotid sinus sensitivity.
4. *Functional alterations in the caliber of the arteries supplying the brain*—vasoconstrictor and vasodilator nervous impulses. Chemical agents including  $O_2$ ,  $CO_2$ , nicotinic acid, alcohol, amyl nitrite, papaverine, ergot and its derivatives, histamine, and adrenalin. Hyperventilation produces vasoconstriction. Effect of tobacco. Influence of warm baths. Physical factors such as missile wounds of neck, carotid puncture, et cetera, can lead to spasm of the carotid vessels in the neck.
5. *The composition of the blood*—anoxic anoxia, anemia, polycythemia, hypoglycemia, dehydration after diuretics, abnormal coagulability of the blood, the effect of anticoagulants on blood flow in small vessels.
6. *Embolism from the site of atherothrombosis.*
7. *The oxygen requirements of cerebral tissues*—cerebral senescence.
8. *Other mechanisms of undetermined nature*—the cause of transient ischemic attacks, stagnant thrombosis, the influence of the emotions (migraine), coughing, direct cerebral carotid sinus reflex, et cetera.

middle cerebral, posterior cerebral, and basilar arteries. These latter vessels supply the deeper cerebral structures including the basal ganglia, internal capsule, thalamus, and brain stem. The small intracerebral branches of the superficial cerebral arteries are also involved. All of these smaller arteries are for the most part spared when the blood pressure is normal, the only exceptions consisting of occasional cases in which the patient is of very advanced age or has diabetes mellitus. Therefore, involvement of these arteries and their territories need be considered in clinico-pathologic deductions only in the presence of high blood pressure.

It is customarily accepted that cerebral thrombosis and arterial occlusion usually occur at the site of the most advanced atherosclerosis. Routine neuropathological examination in our laboratory has shown that this probably holds true for the cerebral vasculature since the above sites of predilection for atherosclerotic deposition proved to be the same regions at which cerebral

thrombosis was most prone to occur. Therefore from a practical point of view it is useful to keep the above scheme in mind when visualizing at the bedside the most likely localization of the vascular disease responsible for the patient's clinical picture.

Having roughly plotted the principle distribution of atherosclerosis along the cerebral arteries, we shall now consider in some detail the manner in which the atherosclerotic plaque can lead to cerebral ischemia, and a resultant disturbance of nervous function. As the plaque progressively encroaches upon the arterial lumen, and the flow of blood to the corresponding territory gradually becomes compromised, the occurrence and severity of local ischemia will be determined in the final analysis, by the interplay of many factors. These can be grouped conveniently under some eight headings as shown in Table II. The flow of liquid in any system is a function of the head of pressure which drives the fluid and the resistance offered by the channels through which the liquid flows; the many factors outlined below are for the most part only an expansion of this simple principle; unfortunately there is not space to consider each in detail.

### Factors Which Determine the Occurrence and Severity of Cerebral Ischemia in Cerebral Atherosclerosis

#### *Degree of Narrowing of the Arterial Lumen.*—

This will be determined or influenced in several ways. First and most obvious is the size of the plaque in comparison with the size of the lumen. Secondly, the effect of the plaque will be greatly increased should thrombosis be superimposed. It has been our experience that uncomplicated atherosclerosis, even of great severity, scarcely ever creates a neurological disturbance if the systemic blood pressure is maintained and the other factors to be discussed below remain constant. Under these circumstances the signs and symptoms of ischemia are produced only if thrombosis be added. The details of the thrombotic process which occurs in association with cerebral atherosclerosis are still incompletely understood. We do not know the circumstances under which thrombosis is initiated nor do we have any accurate idea of the range of speeds with which the thrombus builds up. In some cases it seems that total occlusion can supervene in a few hours, whereas at other times thrombosis appears to be a long-drawn-out process. It is perhaps impos-

sible to obtain accurate data on this question from clinico-pathologic studies, since clinical events are not necessarily closely tied to pathological events in time and also because of the difficulty in assessing the exact age of thrombus material from microscopic examination. However, it is probably correct to say that the effects of a combined atherosclerotic thrombotic obstruction will be influenced by the speed of thrombosis, the extent of its spread along the vessel, and the occurrence of additional clotting of stagnant blood proximally and distally. Finally, it must be remembered that an embolus arising in the heart or elsewhere can become arrested at the point where an atherosclerotic plaque narrows the vessel lumen.

*Availability of Collateral Blood Flow.*—There are several sets of channels through which collateral circulation can become established: (1) the anterior communicating artery from one carotid system to the other or the posterior communicating artery joining the carotid and the basilar system. The pattern of the circle of Willis which is most variable can have far reaching effects on the result of vascular occlusion; (2) the subarachnoid meningeal anastomoses which connect the terminal branches of each major cerebral artery with those of its neighbors, abundant connections existing between the middle cerebral artery on one hand and the posterior cerebral and anterior cerebral arteries on the other (Fig. 2). In addition the larger cerebellar arteries have connections with neighboring vessels of the same and opposite hemisphere; (3) the external carotid artery and ophthalmic artery carry collateral flow in occlusion of the cervical portion of the internal carotid artery; (4) a small amount of blood may enter the basilar system along the cervical branches of the vertebral arteries or via the capillary channels of the labyrinth which is supplied in part from the carotid artery.

The degree to which these channels can enlarge or adapt over a period of time, while an adequate collateral circulation is becoming established, is not known, but in several cases in which they must have been functioning for months or years we did not find gross dilatation on pathological examination. It must be remembered that the development of a collateral flow can be precluded or impaired due to a previous atherothrombosis within the potential anastomatic system, for

example, in the anterior or posterior communicating arteries or in one vertebral artery.

It is important to realize also that although there are excellent anastomoses joining the ter-

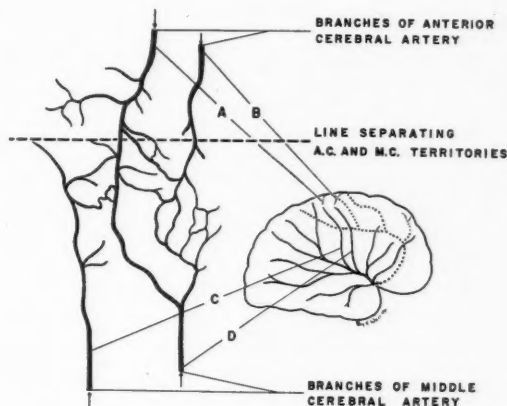


Fig. 2. Drawing of the network of anastomatic vessels connecting the anterior and middle cerebral arteries in the region of the central sulcus. Similar anastomoses are to be found along the remainder of the watershed zone between the major cerebral arteries.

minal arteries of the major superficial cerebral arteries, there is little or no anastomosis between penetrating and superficial vessels, between neighbouring superficial branches of the same artery, and between neighbouring penetrating branches, (the anterior choroidal artery is an exception). As a result when penetrating vessels become occluded, collateral flow other than that which comes via capillaries is not available.

*Maintenance of the Intracranial Arterial Pressure and the Intracranial Blood Flow.*—Of critical importance in this regard is the systemic blood pressure, and not infrequently well-localized neurological signs first develop when myocardial infarction, a massive intestinal hemorrhage, vascular collapse during surgery, or syncope leads to a precipitous drop in blood pressure. This may be due to the presence of a large otherwise silent plaque of atherosclerosis or to the failure of a previously adequate collateral blood flow. Less dramatic variations in cerebral blood flow can result while changing from the recumbent to the upright position, especially immediately after awaking from sleep. In most cases of cerebral thrombosis, symptoms develop during sleep or shortly after arising. The mechanism

responsible for this is not clear, although it is well appreciated that the systemic blood pressure falls during sleep. The cerebral blood flow during natural sleep has not been adequately studied. Oversedation occasionally appears to have been a factor in the onset of a stroke. Hypotensive drugs have been responsible for many cerebral vascular accidents. Some patients with severe atherosclerosis of the carotid sinus develop sinus hypersensitivity and failure of the general circulation can at times be traced to an overactive sinus reflex. Cerebral intermittent claudication in which physical exercise precipitates attacks of cerebral ischemia has been reported in bilateral carotid artery occlusion. The mechanism, no doubt, is a fall in cerebral blood flow due to the upright position and a shift of blood to the active muscle tissue rather than being due to an increase in cerebral oxygen requirement as the term cerebral claudication might imply.

*Functional Alterations in the Caliber of the Arteries Supplying the Brain.*—These may involve the major vessel whose lumen is being occluded and/or the channels carrying the collateral circulation. In animals, stimulation of the sympathetics produces vasoconstriction of the cerebral arteries; stimulation of the vagus, vasodilatation. However, in humans, nervous impulses are commonly regarded as having insignificant influence on the caliber of the cerebral arteries, under both normal and pathological circumstances. There is not time at present to enter into a full discussion of the normal and abnormal vasomotor action of cerebral vessels, a problem which can be epitomized in the popular question, "Does cerebral vasospasm really exist"? Direct observations of human cerebral vessels have been made on only a few occasions and under circumstances which preclude any final judgment as to the existence or not of significant vasomotor changes in cerebral vessels under more or less physiological conditions. To be sure, those who would deny significant "functional" changes in the cerebral vasculature will immediately be faced with the difficulty of explaining the aura of migraine. Many neurosurgeons have encountered cases in which novocain block of the cervical sympathetic nerves has promptly relieved signs of ischemia which had developed in the territory of the carotid artery either as the result of carotid ligation or carotid angiography. Similarly, there have

been several reports in which stellate ganglion block performed soon after the onset of a stroke has produced a dramatic, although often temporary, improvement in the neurological deficit. In some cases, in which worsening occurred as the first block wore off, repetition of the block has again had a beneficial effect.

Changes in the tone of the cerebral vessels are, of course, also produced by various chemicals including oxygen, carbon dioxide, nicotinic acid, aminophylline, alcohol, amyl nitrite, papaverine, ergot derivatives, histamine, adrenalin, and norendralin. The most powerful of the vasodilators is carbon dioxide, inhalation of a 5 per cent carbon dioxide mixture increasing the cerebral blood flow by some 50 per cent. In comparison the other vasodilators (nicotinic acid, alcohol, histamine, et cetera, have only a very weak effect.

Hyperventilation which produces cerebral vasoconstriction has apparently never been used in an attempt to elicit the fleeting prodromal symptoms which often herald the onset of a stroke. The influence, if any, of tobacco smoking on cerebral vessels is not known. Physical trauma such as near-miss bullet wounds can produce extreme vasoconstriction of the extracranial carotid arteries. Likewise, needling the carotid artery or stimulating it electrically also can occasion local spasm of that vessel. Hot baths are said to aggravate focal symptoms and signs in multiple sclerosis presumably by altering the vasculature in some way, but this effect has not been noted in cases of atherothrombosis.

*Composition of the Blood.*—When the circulating blood is faultily oxygenated, threatening ischemia may be aggravated sufficiently for symptoms to appear. Hypoglycemia can lead to local cerebral symptomatology and this may be determined by a preceding local vascular insufficiency. Polycythemia by virtue of increased viscosity of the circulating blood, produces slowing of the capillary circulation, but whether this is of clinical significance is not clear from the available data. Strokes have been reported following the excessive use of diuretic agents presumably due to the production of hemoconcentration. This interpretation, however, needs further confirmation, since the stroke could well be a coincidence. Increased coagulability of the blood, a condition concerning which there is much speculation, might be responsible for thrombosis at the stage of

rather mild atherosclerosis. Conversely, it is almost certain that anticoagulants, both heparin and dicumarol, can in many cases prevent the transient ischemic attacks so commonly seen preceding thrombotic strokes. The mechanism of their action in these cases is not clear as yet, but it has been suggested that in addition to their anticoagulant effect, blood flow through small vessels is enhanced.

*Embolism from the Site of Atherothrombosis.*

—A plaque of atherosclerosis within the carotid artery may rupture and the atheromatous material be widely dispersed distally. A thrombus as it builds up may break away and produce an embolic infarct. Embolic fragments may also be detached from mural thrombus formed upon atherosclerotic plaques within the carotid arteries.

*Oxygen Requirement of Cerebral Tissues.*

This is largely a theoretical consideration and it has not been conclusively demonstrated that normal "use" of the various cortical areas subserving vision, hearing, et cetera, increases the metabolism of these regions significantly above the "resting" levels. In regard to the effect of thinking, Benedict said, "The cloistered scholar at his books may be surprised to learn that the extra calories needed for one hour of intense mental effort would be completely met by the eating of an oyster-cracker or one-half of a salted peanut." This relatively constant oxygen utilization by the brain is in marked contrast to the conditions pertaining in the myocardium where wide fluctuations in the oxygen requirement, due to increased work, may determine the development of a relative ischemia, the coronary blood flow remaining relatively constant.

Under this heading might also be mentioned the influence of preexisting cerebral disease on the effect of ischemia. Elderly persons whose cerebral tissues have been touched by Alzheimer's disease or some other as yet unclassified or unknown "degenerative" process appear to suffer greater damage to brain and mind than younger patients with vascular insults of the same severity. However, this does not mean that the tissues of the elderly are especially susceptible to anoxia, but rather that cerebral functions are already impaired in a way which possibly escapes casual clinical observation with the result that the effect of the added ischemic insult becomes magnified.

*Other Mechanisms of Undetermined Nature.*

(1) The mechanism of the transient ischemic attacks which occur in association with cerebral thrombosis have so far not been satisfactorily explained, and although they probably arise in one or more of the ways mentioned above, some as yet unknown mechanism may be responsible. (2) The changing patterns of blood flow in a complicated network of channels, such as the cerebral arterial tree, can only be surmised at the present time. Some of our observations point to the possibility of local stagnation and temporary cessation of blood flow, particularly in regions of the brain which lie in the most peripheral territories of major cerebral arteries which have become occluded. Here the pressure in the normal artery of supply and in the collateral channels may be approximately equal with the result that blood flow within the intervening territory might become slowed or even cease. An arrangement of this kind would explain some of the unusual pathological findings in so-called cerebral Buerger's disease. (3) The influence of the emotions can also be placed in this group. Not infrequently, the patient will attribute his stroke to an emotional outburst, but the mechanism by which emotion elicits this effect is not understood. Migraine with and without aura provides a good example of the way in which emotional or personality factors can lead to "functional" vascular change. (4) Occasional cases are encountered in which coughing precipitates a fleeting attack of paralysis or numbness and in which the Valsalva effect seems not to be the mechanism involved. (5) The possibility of a direct cerebral carotid sinus reflex must be kept in mind although such cases are rare. The author has not seen an example of this syndrome.

It might seem that the foregoing discussion of the factors affecting the result of atherosclerosis upon cerebral circulation and nervous function is not highly pertinent to the subject of this paper. Certainly, the subject might well have been approached in other ways, for example, by attempting to outline all of the neurological signs and symptoms produced by occlusion of each of the many cerebral arteries, large and small. An undertaking of that nature would have provided an excellent opportunity for a short refresher course on cerebral physiology and cerebral localization; indeed I would have welcomed an occasion to lay before you the fascinations of neurology as

a strokologist. However, no two stroke cases are the same clinically or pathologically. The clinical diagnosis of the nature and location of vascular lesions is not a simple rule-of-thumb matter, and it is a very humbling experience to have one's diagnoses carefully checked at the autopsy table. Well-recognized clinical syndromes associated with the occlusion of various arteries are found outlined in textbooks which nature for the most part seems not to have read, for in actual practice it is much more common to encounter only fragments of a syndrome and those often in such an admixture that identification is most difficult. Rather than attempting an artery by artery account of the clinical picture associated with cerebral thrombosis, I have instead made it my aim to outline some of the general principles which in various combinations are operative in all cases and knowledge of which will help the physician to interpret the interesting series of clinical events encountered in cerebral thrombosis, beginning with the earliest fleeting warning, progressing through the tragic period of the full blown stroke and on to demise or some degree of recovery. The great difference in the clinical course from patient to patient becomes meaningful in some measure only when the principles discussed in the previous section are applied. Furthermore, the use of rational therapeutic methods can for the most part be determined only by a knowledge of the underlying patho-physiological events. An *understanding* of the clinical picture is required for a correct interpretation of our therapeutic successes and failures, and a sound appraisal of the value, if any, of the various kinds of treatment which may be suggested. In the following paragraphs, the practical significance of the above general principles will be further emphasized.

#### Additional Observations Concerning Atherothrombosis

The final part of this paper will be devoted to a number of brief statements concerning some of the more important aspects of thrombotic disease. No doubt at least a few of the conclusions drawn are premature and will require modification in the future, but in general the author has found them useful practical guides at the bedside.

*Atherosclerosis Without Thrombosis.*—In my experience uncomplicated atherosclerosis, even

though severe, does not seem to cause cerebral disease. The plaque is usually placed asymmetrically and a small lumen capable of conducting some blood remains open at one side unless thrombosis takes place. However, should a precipitous fall of the systemic blood pressure occur, ischemia, with or without thrombosis, may follow. The fall in blood pressure can be due to myocardial infarction, hemorrhage, syncope, traumatic shock, surgery and anesthesia, heart block, hypotensive drugs, anaphylaxis, cardiac arrest, carotid sinus sensitivity, et cetera. An occasional exception to the rule concerning the eccentricity of the plaque may be found in the vessels over the cerebral hemispheres in severe hypertension. Then, atherosclerosis may be deposited uniformly around the circumference of the lumen, finally leaving only a threadlike central channel which sometimes extends for several centimeters along the vessel.

*Asymptomatic Cerebral Thrombosis.*—Complete atherothrombotic occlusion is found on pathological examination in cases in which no cerebral lesion can be demonstrated and in which no clinical signs or symptoms had existed. This has been encountered in the common carotid, internal carotid, middle cerebral, anterior cerebral, anterior communicating, posterior communicating, posterior cerebral and vertebral arteries, and on two occasions the basilar artery. On the basis of these findings alone, one must be especially hesitant in attaching significance to plaques which only partially obstruct the lumen. When the middle, anterior, or posterior cerebral arteries become occluded asymptotically, it must mean that the meningeal anastomoses are bringing in an adequate supply of blood from a neighboring artery. At the other end of the pathological spectrum thrombosis in some cases leads to softening and destruction of virtually the entire territory of a vessel. Between these two extremes the infarction resulting from occlusion will vary in site and size according to the interplay of all the factors heretofore described. One can expect, therefore, that the clinical picture and course of recovery will be highly variable.

*Sites of Predilection for Thrombosis.*—Atherothrombosis spares almost no cerebral vessel but corresponding to the special localization of atherosclerosis which was described above occlusion is found in certain regions more commonly than in others. Both the carotid and basilar systems are

frequently affected. In view of the tendency prior to the last few years to airily assign virtually every stroke to the middle cerebral artery, it should be emphasized that the incidence of involvement of the basilar system does not lag far behind that of the carotid. Indeed most stroke cases particularly early in their course should be scrutinized carefully to see if they can be fitted into the picture of vertebral-basilar disease. The vertebral artery may prove to be one of the most frequent of occluded vessels. In order of frequency of thrombotic occlusion the large arteries at the base of the brain might be arranged as follows: internal carotid, middle cerebral, vertebral, basilar, posterior cerebral, and anterior cerebral. When hypertension and atherosclerosis co-exist, the small penetrating arteries will be affected in addition to the large basal arteries. Occlusion of a penetrating vessel results in a small infarct several mm. in diameter in the deeper part of the cerebrum or brain stem and the cystic cavity which remains behind in the healed stage constitutes the so-called lacune. When several of these are present, the term *état lacunaire* is used. These lesions which have not been shown to be clearly due to thrombosis, although that is their most likely cause, are probably the commonest of all thrombotic strokes, and not infrequently at autopsy several such lesions are found in one brain. Lacunes are often the substrate for the brief or mild strokes to which hypertensives are prone and when multiple lesions occur pseudobulbar palsy, dementia, *marche à petits pas*, et cetera, result. The presence of hypertension in the clinical picture indicates, therefore, that the vascular occlusion may possibly be in the smaller vessels, whereas in normotensives this possibility is largely excluded.

*Transient Ischemic Attacks.*—Transient ischemic attacks in which fleeting symptoms come and go are very common in association with atherothrombotic occlusion. Occurring for a variable period before the onset of a stroke, the neurological details of the attack are an accurate forerunner of the form the stroke will finally take and presumably arise as the result of a temporary ischemia which later will no longer reverse itself. There has been much discussion as to the exact mechanism of these episodes, vasospasm, reflex physiologic vasoconstriction of the affected vessel, a fall in systemic blood pressure, undetectable

changes in the pattern of cerebral blood flow, repeated embolization, fluctuation in the size of the thrombus, et cetera, but so far no adequate explanation has been provided. Primary intracerebral hemorrhage practically never gives rise to such episodes and cerebral embolism only very rarely. Therefore, a stroke in which a history of prior prodromal transient attacks can be obtained is immediately stamped as thrombotic in type. Eliciting a careful detailed history of the development of a stroke is one of the most important steps in reaching a conclusion as to the nature of the stroke. Hemorrhage most often comes on gradually over a period of several minutes to an hour or more, while the patient is awake and is not preceded by any type of warning. Hypertension is nearly always present. Cerebral embolism comes on abruptly in most cases and evidence of a source in heart (myocardial infarction, auricular fibrillation, auricular flutter, mitral stenosis, endocarditis, et cetera) and the occurrence of embolism elsewhere in the body substantiate the diagnosis. In saccular aneurysms there is often a stuttering onset associated with headache, loss of consciousness, seizures, and focal neurological signs, but the severity of the headache and the presence of blood in the cerebrospinal fluid will help to establish the correct diagnosis.

The neurological features of the transient ischemic attacks which are encountered in association with thrombosis are not only of several different types but form combinations of the most varied nature. Their character will, of course be determined by the site of the occlusion and also by the many factors which influence the development of ischemia in general. In the middle cerebral artery the attack may be characterized by headache, numbness, paralysis, or paresis of the contralateral side, dysphasia, scintillating scotomata, hemianopia, confusion, and apraxia. Numbness and weakness of the opposite leg, and to a lesser extent the opposite arm, incontinence, apraxia, and confusion may occur with involvement of the anterior cerebral artery. The picture in occlusion of the posterior cerebral artery will be comprised of one or more of the following: blindness, dark vision, scotomata, hemianopia, numbness, tingling, weakness, and confusion. Involvement of the vertebral-basilar system will occasion many different combinations of the following: dizziness, light-headedness, staggering,

veering, diplopia, dark vision, blurred vision, blindness, tubular vision, faintness, unconsciousness, confusion, dysphagia, dysphonia, collapse, weakness of arms and legs, respiratory difficulty, numbness of the extremities of one or both sides, headache, head noises, tinnitus, deafness, twitching, et cetera.

Attacks may last a few seconds up to an hour or more. Repeated attacks usually mimic each other rather exactly and in the intervals between attacks, symptoms and signs usually clear up. Although these transient episodes indicate that a stroke is to be expected, it may be long delayed and indeed sometimes does not eventuate. There may be only one episode before the onset of the stroke, or hundreds or even more than a thousand may occur without a stroke supervening. Warnings may occur for only one day or persist for months and years. The attacks often come on without any recognizable precipitating factors, but not infrequently they will be related to change of posture, exercise, waking up, emotion, standing still, coughing, et cetera. It is our experience that if transient symptoms are found to be present on awakening, the development of a stroke in the very near future is to be feared. In some cases it will be difficult to distinguish transient ischemic attacks from cerebral seizures, Ménière's disease, and migraine, as well as from other types of vascular disease. A proper appraisal of these episodes is of great practical importance since the use of anticoagulants at the stage of fleeting reversible symptoms may allow prevention of a stroke. The time for therapeutic measures is prior to the development of the full stroke, and later no treatment seems to be of avail.

*Development of the Stroke.*—(Only thrombosis is being discussed and not embolism or hemorrhage.) The final development of the full-blown stroke is a most unpredictable matter. Undoubtedly, in some cases, symptoms accrue suddenly and without any recognizable prodrome, the differentiation from cerebral embolism then being most difficult. A common type is that referred to above in which one or more fleeting warnings indicate that disaster threatens. When the final stage is reached the entire neurological deficit may develop abruptly, often during sleep or shortly after arising, or on the other hand, paralysis may come on in stuttering fashion over

a period of several days or even a month, additional fragments of worsening being added from time to time.

Thus, depending on the stage of the illness at which the patient is examined, the physician may ask several questions: (1) Are the fleeting symptoms ischemic attacks or not? (2) Are the transient episodes a harbinger of worse things to come? (3) Is an increasing neurological deficit persisting between the attacks? (4) Is the neurological deficit which the patient now shows all that is to be expected in the near future? This last question is often most difficult to answer and not infrequently a patient admitted to hospital with only weakness of one side or paralysis of one limb or with aphasia, while under observation, is found one morning to have a most severe hemiplegia. When the basilar system is affected, a patient complaining of mild dizziness or dysphagia one evening may be found the next morning in deep coma. There is no satisfactory terminology to indicate this evolutionary aspect of strokes, and at present we use the terms *complete* and *incomplete* stroke to distinguish those in which we think a stable circulatory state has been achieved from those in which a further worsening can be expected.

If anticoagulants given at the stage of the incomplete or partial stroke should prove capable of altering the course of events, it would become a most important matter to be able to recognize the stage at which any stroke stands when first seen clinically. At the present time, we are inclined to feel that when the carotid system is involved, any deficit less than a severe hemiplegia involving face, arm and leg means that further ischemic infarction can be expected in the future, depending on all the factors which determine the degree of ischemia and which were outlined in the previous section. In involvement of the vertebral-basilar system, if the clinical picture indicates that the thrombosis is limited to the vertebral artery, serious progression is not to be expected immediately, although when the other vertebral artery is vestigial or previously occluded, obstruction of the remaining vertebral artery will have the same significance as basilar artery occlusion. When hypertension is a factor a brief, mild stroke may indicate a lacunar lesion rather than a partial stroke, in which case no progression would be anticipated. It should be emphasized that it is impossible in many, indeed

in most instances to predict with any confidence the future courses of strokes-in-evolution.

*Use of Anticoagulants in Atherothrombosis.*—

It is becoming clear that anticoagulant therapy alters the natural course of events in many cases of cerebral thrombosis and postpones indefinitely the arrival of a threatening stroke. However, it is not possible at present to estimate its real value since many strokes which were apparently prevented by giving anticoagulants at the stage of warnings might not have occurred had nothing been done. In some cases transient ischemic attacks have recurred for two or three years and then subsided without resulting in a stroke. There is need of a careful study which will compare the progress of a group of cases receiving anticoagulants with a similar control group in which anticoagulants are not used. Many questions are awaiting an answer: Should all patients exhibiting transient ischemic attacks receive anticoagulant therapy? If not, when does sufficient indication exist? For how long should such therapy be continued? Is excessive hypertension a contraindication to therapy?

From personal experience with a small number of cases, it appears to be quite certain that anticoagulants will in many cases abolish the fleeting attacks which so often herald a stroke. Furthermore, no patient started on anticoagulant therapy at the stage of transient ischemic attacks has gone on to develop a stroke. It is a large undertaking to prescribe anticoagulants in every case in which transient ischemic attacks are present, but at present we think it is justified to consider each patient who has had more than one transient cerebral ischemic attack a candidate for anticoagulant therapy for at least a period of two months. A trial period without therapy is then begun and the patient's future course will determine whether anticoagulant therapy must be restarted. Start and stop therapy is also an excellent method of testing the efficacy of anticoagulants in general. We have had several cases in which symptoms recurred when anticoagulant therapy was stopped, and which cleared when therapy was once more instituted.

Anticoagulants are also indicated when the actual stroke begins to evolve, hoping that the thrombus will diminish in size or that progression can be arrested or delayed while collateral flow is becoming established. Another important group

is that in which a partial stroke or incomplete stroke is present and the prospect of a further bout of worsening is great. These patients should also receive anticoagulants. When speed is essential, heparin and dicumarol are used, otherwise dicumarol alone is prescribed. Patients first seen after the development of a full blown stroke are not given anticoagulants, although it has not been proved that anticoagulants are without benefit even in this type of case. It must be emphasized that we cannot expect all patients to be benefited by anticoagulant therapy since old thrombus will not dissolve and in some cases collateral circulation will never prove capable of compensating for the reduction in flow which resulted from thrombosis. Also it is to be remembered that even though anticoagulant therapy is beneficial at one stage, with the passage of time and the gradual worsening of the atherosclerotic deposition in arteries, a point will be reached at which anticoagulant therapy can no longer rescue the patient from his fate.

*Regarding the History.*—After a stroke has occurred, there may be difficulty in obtaining the details of the development of the illness. When the dominant hemisphere is affected, dysphasia which may be present will often make it impossible to take a history from the patient himself. In non-dominant lesions the patient who is relatively alert may be able to speak clearly and give a satisfactory history. However, in cases with lesions of this type anosognosia is frequently present particularly at the onset of the illness, the patient therefore actually failing to appreciate his illness with the result that the historical details, which were so plausibly presented, prove to be quite false. Therefore, to the obvious difficulty of obtaining a history from a dysphasic patient with a dominant lesion must be added the much less obvious hazard of being misled in cases with non-dominant lesions and anosognosia. The memory function of the elderly is often inconspicuously impaired, making it advisable to have their story corroborated, by younger persons, if possible. Everyone is well aware of the general need for clarity and proper interpretation of the terms used by the patient to describe his illness, but in the case of transient ischemic attacks this need should be especially emphasized. It requires great patience on the part of the clinician if he is to comprehend the exact meaning of the words so

often used by these patients, for example, dizziness, light-headedness, blurred vision, numbness, heaviness, tiredness, headache, noise in the head, et cetera.

*Development of Coma in Strokes.*—The cause of the onset of coma in cerebral hemorrhage is usually quite obvious, namely, a greatly raised intracranial pressure, distortion of brain stem structures, secondary pontine hemorrhages, and often rupture of the hemorrhage into the ventricular system. In cases of brain softening and infarction, the development of coma is not always so easily explained, although extensive involvement of the tegmentum of the brain stem in the basilar territory characteristically leads to deep coma. When either cerebral hemisphere is affected, profound unresponsiveness developing over a few days is not due to "extension of the clot," an explanation so frequently offered, but usually is the result of brain swelling and herniation of brain tissue through the tentorial opening, under the falx, or into the foramen magnum. Unsuspected extensive involvement of both hemispheres is another possibility. Uncomplicated softening in the middle cerebral territory of one hemisphere will in most cases not produce deep coma.

*Headache.*—It is not widely appreciated that headache or head pain frequently accompanies cerebral thrombosis. Although this type of headache has not been studied in detail a few observations may be recorded. Certainly it does not accompany all thrombotic strokes or even the majority. Usually the headache is mild but definite, and only rarely is it a prominent complaint. In involvement of the internal carotid artery the pain is most often above the corresponding eye but may extend posteriorly over the side of the head. Thrombosis of the posterior cerebral artery is referred forwards to the anterior and lateral frontal regions. In disease of the basilar artery, headache is usually mid-line in the occipital region. Vertebral artery pain is referred to the area behind the mastoid process. Headache not infrequently occurs with transient ischemic attacks. The headache most often is deep and steady, but occasionally it is throbbing in character.

*Dementia.*—The mental deterioration of senescence both in its mild and more aggravated forms

is often attributed to cerebral arteriosclerosis or "hardening of the arteries" without any clear idea of the underlying pathological picture or the pathophysiological implications of such a statement. Mental decline in which the clinical picture is characterized for the most part by impairment of memory is usually a reflection of Alzheimer's disease or some other "degenerative" process of undetermined nature, conditions in which impaired cerebral blood flow and cerebral infarcts play no part as far as is known. On the contrary, when cerebral atherosclerosis produces dementia it usually does so by causing ischemic infarcts which are so located as to damage those parts of the brain especially subserving mental function. In most instances, therefore, it will be possible to discover in addition to mental deterioration, focal neurological signs which will suggest the presence of vascular disease. Dysphasia, apraxia, hemianopia, hemiparesis, altered tendon reflexes, or abnormal plantar responses, may be found. Furthermore, the onset is liable to be abrupt when infarction is responsible, whereas in the degenerative processes mental recession is usually quite gradual. The concept that undiscovered small strokes in "silent" areas are responsible for mental decline is an attractive one, but further clinico-pathologic studies are awaited before it can be accepted. In our experience, mental deterioration clearly attributable to cerebral atherosclerosis usually is accompanied by tell-tale neurological abnormalities.

*Cerebral Thromboangiitis Obliterans.*—The pathological condition which goes by this name is characterized by sunken yellowish brown areas of old infarction scattered continuously or discontinuously over the cerebral hemisphere, especially in the watershed region separating the middle cerebral territory from that of the anterior and posterior cerebral arteries. A unique feature, however, pertains to the arteries within the infarct which are reduced to white threads. The lumen of these vessels is filled with a fine connective tissue meshwork. Although there is no arteritis, the name thromboangiitis obliterans was applied because of the resemblance of the vessels to those described by von Winiwarter in the arteries of an amputated foot. In several cases described in the literature, a large artery, internal carotid, middle cerebral or anterior cerebral, was also occluded, but this was felt to be

co-incident. In our material, similar occlusions of large vessels (internal carotid, middle cerebral) have been found in most instances and it is suggested that the characteristic cerebral lesion is not related in any way to thromboangiitis obliterans (itself an ill-defined entity). On the basis of the location of the infarct far peripherally in the middle cerebral territory and the intervention of rather healthy patent artery between the white occluded portion and the occlusion more proximally in the larger parent vessel, it is suggested that intravascular clotting occurs due to the local stagnation of blood when the pressure in the main artery of supply balances the pressure in the collateral channels. The fine connective tissue which fills the lumen of the white

worm-like arteries is the result of the organization of blood clot. There has not been any evidence of arteritis in our cases and the designation of the lesion as an angiitis is quite unwarranted.

### Summary

1. A résumé of cerebral arterial disease has been presented.
2. Some of the pathological aspects of cerebral atherosclerosis have been described.
3. Some of the factors which influence the local cerebral blood flow distal to an atherosclerotic plaque have been briefly outlined.
4. Several aspects of cerebral atherothrombosis have been dealt with, particularly the more important clinical features.

### Discussion

A. B. BAKER, University of Minnesota: Dr. Fisher has presented a very excellent review of the subject of cerebral arteriosclerosis. One must certainly agree with most of his opinions and observations. In his discussion, Dr. Fisher has emphasized primarily the involvement of the larger basilar vessels since these structures are most commonly implicated in those patients who are considered to be suffering from the striking syndromes of cerebral thrombosis. Generally the smaller intracerebral vessels, those under 100 microns, are not given too much consideration, particularly in individuals who are normotensive. We have been much more impressed by the changes in these vessels, particularly in individuals who do not show evidence of hypertension.

These smaller intracerebral vessels always show a constant structural alteration with age. As early as the third and usually during the fourth decade of life, these vessels from 20 to 150 microns in diameter begin to show changes in their structure. The elastica interna becomes reduplicated, fragmented, and often loses its normal tinctorial properties. The media undergoes fibrosis with hyalinization and occasionally calcification of

some of its elements. Often by the fifth and sixth decades, these vessels show indistinct staining of all the medial elements and a definite narrowing of the vessel lumen. We have examined a large number of brains of normotensive individuals in which this narrowing has resulted in tiny areas of perivascular tissue change. These changes within the smaller intracerebral vessels are variable in degree but definitely increase with age. Certainly within the older age groups namely the fifth and sixth decades, the intensity of alteration and the degree of vascular narrowing is quite variable.

In view of the fact that these changes within the smaller intracerebral vessels are always present and progressive, one wonders whether they may not be playing some role in the final clinical picture seen in the thrombosis of the larger basilar vessels. May not the final clinical picture in the obvious cerebral thrombosis, and perhaps some of the variability in the clinical symptoms as well as the ultimate prognosis, be modified or influenced by the changes that normally occur within the smaller intracerebral arteries?

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"As doctors and clinicians, our problem is to balance beneficial effects of ovary removal against the loss to the patient of orderly hormone interchange, plus the loss of protective action of ovarian secretion. From the standpoint of the heart specialist, the harmful effects on the circulatory system outweigh the possible beneficial effects, except in the exceptional instance," Dr. George C. Griffith told some 1,200 doctors attending the fourth annual clinical meeting of the American Academy of Obstetrics and Gynecology, in Chicago.

Dr. Griffith said the practice of removing ovaries, usually in the course of other pelvic surgery, in women

who have passed the child-bearing age is based on the old and erroneous belief that the glands are useless by that time and that their removal prevents possible development of ovarian cancer, which strikes down one woman in each 100 women past the fortieth year.

There is a growing realization that the ovaries are not concerned only with the sexual and reproductive life of the individual, but, continued Dr. Griffith, among the other important functions of the ovary is the regulation of metabolism. Furthermore, in cases of impaired pancreatic activity, ovarian hormones protect against diabetes.

# *The Internist and Some Tools*

## **Arteriosclerosis in African Populations**

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**M**Y PARTICULAR task is to review the available evidence on the incidence of arteriosclerosis in different populations in the African Continent with particular reference to whether differences in incidence can be related to genetic or environmental differences between populations.

The term arteriosclerosis is used in a very broad general sense to cover all forms of degenerative sclerosis of the arterial tree. The term atheroma is used to cover the well known degenerative lesion of the intimal and immediate sub-intimal tissues. Atherosclerosis is used to cover a related condition in which the process involves the media as well as the intima. It is typically seen in the advancing years of life (decreased arteriosclerosis) and may or may not be associated with hypertension, renal disease or diabetes. The term Mönckeberg's arteriosclerosis is used to cover a group of cases in which calcification is widespread and radiologically visible in the large and medium sized arteries.

These four disorders are not clearly demarcated and merge into each other. They may all be idiopathic and normotensive, but may all be associated with (1) idiopathic hypertension (2) renal hypertension (3) diabetes.

All forms of arteriosclerosis may vary in the extent to which they affect respectively the aorta, the coronary arteries, the renal arteries, the arteries of the limbs, the cerebral arteries, and the pulmonary artery and its branches. There is also a variation in the respective incidence on large, medium and small arteries.

All the factors discussed above must be taken into consideration in attempting to compare the

incidence of arteriosclerosis in different populations.

This communication will be confined to Africa south of the Sahara (a WHO region). The two main population groups in this region are Negro and Bantu. Hailey<sup>1</sup> (1938) describes the peoples of Africa as deriving from three principal stocks, Bushmen, Negro and Hamite. The Hamites are represented mostly north of the Sahara but the so-called Eastern Hamites probably invaded Africa in successive waves from Southern Arabia. The Bantu group arose from modification of a predominantly Negro race by the Hamitic influence (see map). They spread westward and southward but mainly south of the Bantu line which is never very far from the equator. The term Bantu is mainly linguistic in its significance but is associated with certain cultural traits of Hamitic origin. These people had been migrating southwards from the equator and had largely displaced the original Bushmen-Hottentot mixture of southern Africa before they met the European invading the continent from the south. Hamitic influence is absent or slight in the Negro migrations north of the equator which peopled West Africa and from which presumably the Negro people of the United States derived.

There remain small pockets of distinct and probably more primitive peoples in the Congo basin (Pygmies) and in the Union of South Africa (Hottentots and Bushmen). Europeans born and reared in the African continent are almost confined to the so-called White Highlands of Kenya and Southern Rhodesia and to the Union of South Africa. In the Union of South Africa there are approximately a million Cape Coloured people who are more or less culturally and racially homogenous on a European rather than African pattern (Brock<sup>2</sup> 1949).

Their derivation is mainly from the original

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Hottentot inhabitants with considerable admixture of slaves brought from Indonesia and Malaya and also with promiscuous whites. From our point of view it is important that they are genetically distinct from the Bantu.

Study of the sickling phenomenon, the ABO and other blood groups, and the different hemoglobins is beginning to throw interesting light on racial origins in the African continent, but so far none of these new data have been correlated with the problem of arteriosclerosis.

Among the background publications on interracial variations two books should be specially mentioned, namely, "The Biology of the Negro" by J. H. Lewis<sup>3</sup> (1952) and "Civilization and Disease" by C. P. Donnison<sup>4</sup> (1937). The first is a general study of the appearances of disease in the American Negro. The second is a general study of world trends in disease from the particular point of view of one who had spent considerable time in the practice of medicine in Central Africa.

Published information on the subject under review from Africa is fragmentary and scattered. It has been supplemented by correspondence with internists and pathologists in certain centers whose opinions are acknowledged as personal communications. In the last year or two, under the influence of increasing interest in the relationship between diet and atherosclerosis and the blood lipoproteins, reports have been published by Walker, Higginson et al<sup>5,6</sup> from Johannesburg (1954) and an intensive study of three population groups in Cape Town has been carried out by a team directed by the authors. The methods used have been correlated with those used by Ancel Keys who with Mrs. Margaret Keys spent a month in Cape Town in the survey. Results of this survey will be referred to as the Cape Town survey. Acknowledgment is made to those who participated.\*

It is our intention to take as a starting point the two papers published from Johannesburg in 1954 and to proceed both forward and backward from this starting point. The forward progression will confirm and expand the Johannesburg work from the experience of the Cape Town survey and will show that, using identical techniques in a single climatic and geographical environment, markedly different experiences of coronary thrombosis are found and show linear correlation with differences in serum cholesterol and lipoproteins and with dietary fat intake.

The historical review will attempt to show that coronary heart disease, at least among primitive peoples, does not necessarily show close correlation with other forms of arteriosclerosis, and



The African continent showing the WHO African Region (south of the Sahara) the Bantu line (wavy line cutting across the equator) and the borders of the Union of South Africa.

\*The Cape Town Coronary Heart Disease Survey: This survey was carried out within the municipal boundaries of the City of Cape Town from March to May 1955. It was directed by John F. Brock, professor of medicine in the University of Cape Town, and organized by B. Bronte Stewart, assistant physician at the Groote Schuur Hospital on the Joint Medical Staff with the University of Cape Town. Other medical contributors include B. Kaplan (medicine) and R. Singer (anatomy). Miss A. Moodie, research social worker in the Department of Medicine, played a very active part in the organization and conduct of the survey, and A. Antonis, Ph.D., organized the laboratory work. Acknowledgment is made to the technicians and secretaries whose enthusiasm and hard work made the survey possible and to the representatives of many employing bodies who assisted in the provision of human volunteers. Acknowledgment is made finally to Ancel Keys and Mrs. Margaret Keys for their assistance in the organization of methods and standards and for their very hard work during their stay in Cape Town. The survey was financed in part by the S. A. Council for Scientific and Industrial Research through the budget of its Research Unit in Clinical Nutrition directed by Professor Brock; in part also by research funds provided through Ancel Keys.

that the problem of coronary heart disease needs to be considered separately from the problem of arteriosclerosis in general.

In the historical review it will be necessary to refer to articles in journals that are not well known to American readers and some of which may be difficult of access. It may be an important part of our contribution to list some of these titles so that they can be consulted by those who wish to get at the original facts,

To summarize first the 1954 contribution from Johannesburg, there are companion papers by Walker and Arvidsson<sup>5</sup> and by Higginson and Pepler.<sup>6</sup> The first paper shows that the blood cholesterol level of the Johannesburg Bantu is low compared with European standards and that the fat intake in the diet is low. The second paper deals with atherosclerosis and coronary heart disease in the same group of people. It should be emphasized that the authors confine themselves to a study of the coronary arteries and the aorta. They analyzed 523 unselected necropsies performed under the supervision of one pathologist at Baragwanath Non-European Hospital. Atherosclerosis was classified according to the grading of Wanscher, Clemmesen and Nielsen<sup>7</sup> (1951). In this series there were 150 deaths from cardiovascular disease (including tuberculous pericarditis): eighty-four men and sixty-six women. Of these cardiac deaths only eight (four men and four women) were attributed to coronary disease.

They compare the incidence of the severer grades of atherosclerosis (grades 3 and 4) in their Bantu series with the findings by the same grading in the Danish series of Wanscher, Clemmesen and Nielsen and the difference is most striking. For example, among men in the age range 40-49 the incidence of grade 3 atherosclerosis was 3 per cent in the Bantu series and 32 per cent in the Danish series, and of grade 4 1 per cent in the Bantu series and 8 per cent in the Danish series. They tried to use the same grading as the Danish workers but comment that "it is probable that several cases graded as 3 or 4 in this would have been graded less by the Danish workers." The Danish authors for example described the coronary arteries in grade 4 as being "transformed to stiff and narrow chalky pipes without elasticity" but they feel that not a single case graded as 4 by them could be justifiably so described.

In the same paper they refer to a larger series

of 1,328 consecutive necropsies carried out by various members of the staff at the same Hospital over a period of five and one-half years and which includes the smaller series of 523. In this larger series there were seven cases of coronary thrombosis or myocardial infarction and one case in which the diagnosis of ischemic heart disease was considered tenable.

A most important publication on arteriosclerosis in the Bantu and Coloured races of South Africa is a series of articles by Becker<sup>8</sup> (1946). This is a most exhaustive study by a pathologist in Johannesburg of "cardiovascular disease in the Bantu and Coloured races of South Africa." The distribution of the races is given in the first paper. It covers the various Bantu tribes of Southern Africa but includes 17 per cent of Coloured people, referred to by Becker as Euraficans. This latter group is very similar to the group described in the Cape Town survey as Cape Coloured people, but probably has more Bantu blood.

Writing on atheromatosis, Becker states:

"The incidence of atheromatosis in the ascending period of life in Bantu and Coloured subjects is not far removed from that in other races; the incidence of the senescent type may be slightly less. Pathological effects of atheromatosis are limited to the senescent type. The lesions tend to occur particularly in those with hypertensive heart disease."

When discussing heart disease, he says:

"The general incidence of hypertensive arteriosclerosis is judged to be rather less than that which is found in the American Negro and rather more than in the white races of the United States. There is a steadily rising incidence with advancing age reaching a maximum in the sixth decade of 15 per cent. It is the commonest cardiovascular disease among the Bantu and Coloured people, being responsible for one third of all cases of congestive failure and for nearly 6 per cent of all deaths. In spite of the fact that the coronary vessels are frequently diseased in the condition, and the myocardium is frequently gravely damaged, coronary thrombosis is an uncommon lesion. Similar conclusions have been arrived at in regard to the Coloured races in America."

An excellent recent general review which will not easily be available to American readers is that by Elliot<sup>9</sup> (1953). This study is entitled "Coronary Arteries and Their Diseases in the Bantu." The author discusses the rarity of coronary heart disease in Bantu from three angles, namely, ex-

perience of myocardial infarction, of cardiac aneurysms and of sudden deaths.

*Myocardial Infarction.*—Elliot had no proved cases admitted over a two-year period to 150 medical beds for non-European patients in Johannesburg. (One suspected case was found at autopsy to have syphilitic coronary ostial stenosis; one was discharged and not seen again).

Grek analyzed 6,000 Bantu patients passing through sixty-five medical beds in a period of six years. Of twenty-two cases initially diagnosed as myocardial infarction fifteen were later reasonably attributed to syphilitic coronary ostial stenosis. Of the remaining seven only three were followed to autopsy, and of these three only two were reasonably attributed to coronary thrombosis. At the same time and place in 8,000 admissions to the European Medical Wards of the Johannesburg General Hospital 1950-1951 there were 235 cases of coronary thrombosis with myocardial infarction.

*Cardiac Aneurysms.*—Over a twelve-year period at the Johannesburg General Hospital, the adjoining Non-European Hospital and at the Johannesburg Medico-Legal Laboratories there were fifty-seven European and fifteen Bantu cases of cardiac aneurysm. Among the fifty-seven European cases severe grades of coronary atherosclerosis were noted in every case, whereas in the fifteen Bantu cases no notable coronary atherosclerosis was found. The peak incidence for the fifty-seven Europeans was 60-69 years, whereas among the fifteen Bantu it was 30-39 years. In ten of the fifteen Bantu cases, other causes were found for the aneurysm. These were syphilis of the cardio-vascular system, six; tuberculosis of the heart, one; mycotic aneurysm, one; congenital myocardial defect, one, and Loeffler's parietal endocarditis, one. In the remaining five cases the cause of the aneurysm was not definitely established. The slight atheromatous changes could not reasonably be regarded as causative.

*Sudden Deaths.*—Elliot quotes figures for a six-month period at the Johannesburg Medico-Legal Laboratories. Forty-two European deaths were all due to myocardial infarction resulting from coronary thrombosis. Of forty sudden deaths in Bantu none were due to coronary thrombosis or myocardial infarction. The age range for

the Bantu sudden deaths was of course much lower than that of the European sudden deaths.

*Arteriosclerosis in General.*—In marked contrast to the apparent rarity of coronary heart disease and of severe coronary atheroma in the Bantu is the comparative frequency of hypertension and of arteriosclerosis of other forms. Elliot's analysis can be summarized as follows:

*Hypertension.*—Ordman<sup>10</sup> (1948) examined the blood pressure of 1,522 Bantu subjects in urban and rural areas scattered over South Africa and found hypertension in about the same frequency as in the European.

Grusin and Gillanders examined 1,000 urban Bantu subjects in Johannesburg and concluded that hypertension in the Bantu is about as common as in the North American Negro. Ordman<sup>10</sup> and Becker<sup>8</sup> (1946) review the subject of hypertension in the non-European races of the world.

*Arteriosclerosis, All Forms.*—Elliot quotes J. C. Gilroy, V. H. Wilson, A. B. Gillanders and I. J. Grek, all of whom are experienced in Bantu medicine in Johannesburg, as agreeing that all forms of arteriosclerosis including atherosclerosis and Mönckeberg's sclerosis are common in the Bantu. Cerebral thrombosis and hemorrhage based upon hypertensive atherosclerosis are not uncommon but are perhaps a little less common than in the European. Hypertensive retinal changes of all degrees are equally common in both races. Hypertensive nephrosclerosis is probably more common in the Bantu and more severe in its effects. Peripheral vascular disease is not uncommon.

On the subject of Mönckeberg's sclerosis Elliot is quoted above as saying on the authority of several experienced people in Johannesburg that all forms of arteriosclerosis including atherosclerosis and Mönckeberg's sclerosis are common in the Bantu. Evidence has been sought from radiologists as to the incidence of recognizable calcification in the aorta and arteries of the lower legs in Bantu subjects. The impression is that it is uncommon but there is not enough evidence on which to base a firm opinion.

In our recent survey of approximately 600 adult males under age sixty in Cape Town, we found that the proportion exhibiting blood pressures

over 145/90 was not significantly different (15.6 per cent European, 21.9 per cent Coloured, 20.4 per cent Bantu) in our three racial groups which were similar with regard to mean age and sample size.

From Salisbury in Southern Rhodesia, Gelfand<sup>11</sup> (1952) reports that in 1,500 consecutive admissions to his Bantu Hospital Wards in the last eighteen months, seventy (4.67 per cent) had systolic pressures above 150 and 101 (6.73 per cent) had diastolic pressures above 90. Unfortunately, the ages of his patients are not recorded and it must be remembered that the average age in one of his wards would be very much lower than in the average European Hospital Ward. In the same paper he quotes his own experience of the variety of heart disease in his Bantu medical wards. Among 189 cases of heart disease of all types (114 male and seventy-five female) hypertensive cardiac disease was found in twenty-eight (14.81 per cent). This can be compared with the incidence of other types of heart disease in this series; rheumatic heart disease, fifty-one (26.98 per cent), nutritional heart disease, twenty-nine (15.34 per cent), essential hypertension, twenty-eight (14.81 per cent), syphilitic heart disease, twenty (10.53 per cent), congenital heart disease, seventeen (8.94 per cent), anaemic heart disease, eleven (5.82 per cent), tuberculous pericarditis, nine (4.76 per cent), cor pulmonale, seven (3.7 per cent), arrhythmias, seven (3.7 per cent). In this series coronary heart disease, sub-thyroid heart disease and beri-beri were not encountered. He comments, "It may be safely stated that coronary heart disease (coronary thrombosis and angina pectoris) is extremely rare in the African."

An important series of contributions to knowledge of arteriosclerosis in the African comes from East Africa and particularly from Kampala, Uganda. Williams<sup>12</sup> (1944) in a series of papers laid the foundations while Davies<sup>13</sup> (1948) gathered up the clinical experience of Williams and his own experience as a pathologist in Uganda. Davies says that his experience in Uganda is similar to that published by Vint<sup>14</sup> (1937) who found that "minor degrees of atheroma of the aorta were general in Africans in Nairobi after the age of eighteen years, but in only 8.9 per cent of cases was the lesion well marked." At Mulago Hospital in Kampala, Uganda, Davies found "minor degrees of athero-

ma of the aorta were common, while in thirty-eight out of 2,994 autopsies an advanced degree of atheroma was present." Particulars for age are incomplete but of the thirty-eight cases twenty-four had an average age of 46.6 years. Davies says that "apart from their infrequency, the arteriosclerotic lesions were exactly similar to those found in Europeans." He comments also that "one of the most puzzling features of atheroma in Negroes is the rarity of coronary thrombosis." In the late 1930's various workers in East Africa had commented (Donnison, C. P.,<sup>4</sup> 1937; Vint, F. W.,<sup>14</sup> 1937; and Hennessey, R. S. F.,<sup>15</sup> 1938) on the comparative rarity of hypertensive heart disease and cardiovascular hypertrophy. Comparing the later work of Williams in Uganda and of Becker in Johannesburg Davies concludes that "the careful work of Williams and Becker suggests that the earlier views were ill-founded and that hypertensive disease is nearly as important to the African in Africa as it is to the African in America."

Williams<sup>16</sup> (1955) writing recently from Uganda says, "With regard to coronary infarction and angina of effort, my experience is entirely negative. I have never yet made a clinical diagnosis of coronary infarction in an East African which has been corroborated post-mortem. As anyone who knows Mulago Hospital will believe this is not for lack of autopsies. The occasions on which I have entertained a clinical diagnosis of coronary disease in a local African have been exceedingly few; not only is the negative autopsy experience a deterrent, but I have so rarely met with anything resembling cardiac pain in African patients here. I shall not be a bit surprised if this situation should alter in the next few decades. It is altering so radically already in some connections, e.g., peptic ulcer. I no longer regard African medicine as static."

Davies<sup>18</sup> (1955) has recently confirmed the above views in the following words: "While mild degrees of atheromatosis are not uncommon, a severe degree of atheroma contributing to heart failure is uncommon in East African natives although more common in the South African Bantu." He adds to this, "I have never seen a case of coronary thrombosis in an African here, and know of only one in our records since 1931. Atheroma of the cerebral vessels is very rare. Mild aortic atheroma is seen, but very rarely is there severe atheroma unless syphilis is present."

From West Africa Edington<sup>19</sup> (1954) confirms the low incidence of myocardial infarction in the West African Negro. In an analysis of 3,645 autopsies performed at Accra, Gold Coast Colony, during the years 1921 to 1953 he found a low incidence of cardiovascular disease. This he thought could be accounted for in part by the smaller number of autopsies in the older age groups but expressed the opinion that it is due also to the low incidence of coronary disease. Disease of the coronary arteries was considered to be the cause of death in only thirty cases (6.4 per cent of cardiovascular conditions).

The foregoing evidence shows a striking immunity of the Bantu and Negro peoples of Africa to the effects of coronary occlusion. Although their life expectation is considerably less than that of the European, the immunity is evident in the decade thirty to forty years and is too great to be attributed to lesser life expectation. This opinion is confirmed by exact figures quoted later for comparison of three racial groups in Cape Town. There is evidence, particularly in the work of Higginson and Pepler<sup>6</sup> (1954), that this immunity may be due to a considerably less severe degree of coronary atheroma in these African people than in Europeans. In view, however, of the fact that Africans are by no means free of some of the other manifestations of arteriosclerosis and hypertension it would be unwise to ignore other factors that may account for their immunity to the effects of coronary heart disease.

The factors which need to be considered seriously are:

1. The possibility that the African is genetically endowed with a coronary artery system which allows a freer anastomosis between the different branches, and therefore a lesser tendency to ischemia even in the presence of severe narrowing of a coronary artery.

2. That the African possesses an inherent or genetically determined peculiarity in cholesterol metabolism that protects him from coronary atherosclerosis.

3. That either for genetic or for environmental reasons the African has a lesser tendency to intravascular clotting in the coronary arterial system even in the presence of coronary atherosclerosis.

*Anatomical Differences in Coronary Arterial Tree.*—Brink<sup>20</sup> (1949) studied the possibility of a different coronary artery pattern in the Bantu. He claimed that in the Bantu there is an especially developed third primary division of the left coronary artery. This subject was fully discussed by Elliot<sup>9</sup> (1953) who concluded that "the finding of a difference in the Bantu and European coronary artery pattern is certainly of social and anthropological interest. The differences that have so far been demonstrated appear to have little if any bearing on the incidence of coronary artery disease and disease syndromes, the peculiarities of which in the South African Bantu remain an unsolved problem." This opinion is supported by the preliminary finding of Singer<sup>21</sup> (1955) who has found the same coronary branch anomalies in European hearts. A genetic difference in coronary vascular supply cannot at present be finally excluded as the cause of the African's immunity to coronary heart disease but it would be unwise to give this possibility serious consideration until the effects of environmental factors have been excluded.

*Inter-racial Differences in Incidence of Thrombo-Embolic Phenomena.*—An uncompleted inter-racial study at present in progress in Cape Town has concerned itself with blood clotting mechanisms.<sup>47</sup> This study was initiated in order to determine whether the Bantu possessed differences in clotting time to account for the widely held view that thrombo-embolic phenomena are rare in this ethnic group. In view of the findings of Strom and Jensen<sup>22</sup> (1951) on this aspect during the war years in Norway it seems highly probable that environmental and not genetic factors are at play. The decline in death rate in Norway during the war years occurred rather too suddenly to be accounted for by resolution of atheroma if such is possible. Furthermore the views of Morris<sup>23</sup> (1951) on the unchanged severity of coronary atheroma over the last four decades again emphasize that more attention should be paid to intravascular clotting in determining the effects of coronary heart disease.

*Inter-racial Differences in the Incidence of Coronary Heart Disease and the Mean Levels of Serum Cholesterol in Cape Town.*—We cannot subscribe to the view that the geographic or climatic environment in any way accounts for the

## AFRICAN POPULATIONS—BROCK AND BRONTE-STEWART

TABLE I. MEANS AND STANDARD DEVIATIONS FOR CLINICALLY HEALTHY MEN AGED 40 TO 58 YEARS IN THE CAPE PENINSULA

	Bantu	Coloured	European
No. of Subjects	132	118	114
Mean Age	45.8 ± 5.5	46.5 ± 5.0	47.0 ± 5.2
Mean Total Serum Cholesterol	166.3 ± 47.2	204.1 ± 54.8	234.0 ± 52.9
B			
Cholesterol			
Lipo-Protein			
mg per 100 ml			
Fraction	122.3 ± 47.9	160.5 ± 54.4	194.5 ± 52.8

All of the differences shown (except mean age) are statistically highly significant.

differing incidence of coronary heart disease and the different levels of serum cholesterol that have been reported from studies on different populations. Europeans in South Africa whose mode of life is not unlike that of individuals of Western European descent residing in Western Europe and Northern America possess a mean serum cholesterol and death rate from coronary heart disease not unlike that of the Northern American. In Cape Town the death rate ascribed to coronary heart disease in the individual of pure European descent is more than twice that of the Cape Coloured in the age group thirty-five years and over (M.O.H. Annual Report<sup>24</sup> 1946). In the Bantu townships of this city, the registration of a death as being due to coronary heart disease is an exceedingly rare occurrence. Possibly one to three are registered per year (M.O.H. Annual Report<sup>25</sup> 1925) in an estimated population of over 100,000 Bantu. The comparative rarity of the disease is reflected in our hospital statistics, clinical observations and post-mortem studies. Vogel-poel and Schrire<sup>26</sup> (1955) recently have analyzed over 5,000 electrocardiograms taken on adults at the Cardiac Clinic at Groote Schuur Hospital. This hospital caters for the poorer section of the community of Cape Town and the hospital attendance figures shows a bias in favour of the non-European. Despite this, of the 550 classical myocardial infarction electrocardiogram patterns, 448 were in Europeans, 100 in Cape Coloured and only two in Bantu: The numbers of electrocardiographs requested by physicians for the different racial groups are very different indicating a greater expectation by physicians of abnormal patterns in the European than in the non-white groups. When the figures are expressed as myocardial infarct patterns per 100 electrocardiographs taken on each racial group the figures are European 13.54, Cape Coloured 6.80, Bantu 0.9.

TABLE II. STANDARDISED MORTALITY RATIOS OF MEN AGED 20-64 (1950) GREAT BRITAIN

	Social Class				
	I	II	III	IV	V
Coronary heart disease	150	110	104	79	89

Standard mortality ratio may be defined as the number of deaths occurring among men aged 20-64 in a given occupation expressed as a percentage of the number of deaths that might have been expected to occur if the given occupation had experienced within each age group the same death rate as that of a standard population consisting either of all males or of all occupied and retired males only. Constitution of the social classes is I—professional etc., II—intermediate, III—skilled, IV—partly skilled, V—unskilled occupations.<sup>28</sup>

When they are analyzed per decade of age from 30 to 59 years the distribution is not significantly different for white and combined non-white people. These figures should dispel any lingering inclination to doubt the remarkable immunity of the Bantu people to myocardial infarction. The geographic or climatic environment cannot explain these wide differences between the European and non-European populations in Cape Town. Other environmental factors must be at play.

Cape Town is favourably situated for an inter-racial study as each race in the main, still adheres to its traditional customs. Consequently a large number of environmental factors become available for study. During March to May, 1955, we sampled approximately 200 working adult males under the age of sixty years, from each of the three main racial groups, to study some of these environmental factors. The study involved clinical, electrocardiographic, anthropometric, socioeconomic, hematological and bio-chemical examinations. A summarized version of the results in the middle aged group now follows.

Of the 383 men aged between 40 and 58 years there were only nineteen exclusions due to probable ill health. One European had xanthoma tuberosum, there was one diabetic in each racial group and the remaining fifteen were excluded on clinical or electrocardiographic evidence of probable present or past experience of coronary heart disease. Commensurate with our clinical and hospital experience the proportion of these fifteen exclusions in Bantu, Cape Coloured and European was respectively 1 to 5 to 9. Furthermore the one Bantu had doubtful electrocardiographic changes only.

The mean serum total and  $\beta$  lipoprotein chole-

terol levels for these three ethnic groups of like mean age show a pattern with the Bantu at one extreme and the European at the other. The Cape Coloured lie in-between (Table I). The differences are highly significant ( $P < 0.001$ ). The problem immediately arises whether these cholesterol differences are due to genetic or to environmental differences between the three racial groups.

Over the last two decades evidence has accumulated that wide differences in susceptibility and whether the differences in coronary heart disease have the same cause.

to coronary heart disease and different levels of serum cholesterol have occurred not only between ethnic groups but also within a given ethnic group. The last world war contributed greatly through the changing mortality experience (Strom and Jensen<sup>22</sup> 1951) and changing serum cholesterol levels (Schettler<sup>27</sup> 1950) in Europe. This is also illustrated by the decennial occupational mortality statistics of England and Wales (Registrar General<sup>28</sup> 1954). This publication shows the susceptibility of the professional and executive classes in particular (Table II). The fact that a similar trend exists in wives over sixty-five years of age and in retired men suggests that socio-economic factors are of greater importance than the nature of the occupation. Of the many social factors, economic privilege becomes the most outstanding.

It was of interest to us to study whether economic privilege affected the serum cholesterol pattern within each racial group. Subdivision into what could be considered as high, middle and low income levels for the particular ethnic group led to a very wide inter-racial economic range with low income Bantu at one extreme earning less than eight dollars a week to high income. Europeans earning 100 to 200 dollars a week. Within each ethnic group the more privileged economically had higher mean serum total and especially  $\beta$  lipoprotein cholesterol levels (Fig. 1). Genetic racial influences now appear less important when one notes that individuals on the same economic plane, irrespective of their racial origin exhibit similar cholesterol levels.

Apart from income, many other environmental factors, some related to the socio-economic status, distinguish our three ethnic groups. Many of these have at some time or another been advanced as factors in the pathogenesis of coronary heart disease. Amongst these, exposure to infection, the degree of physical and mental activity, the

consumption of alcohol and tobacco, obesity and the diet have all received consideration in this survey. The detailed results have been published elsewhere (Bronte-Stewart, Keys and Brock<sup>29</sup>

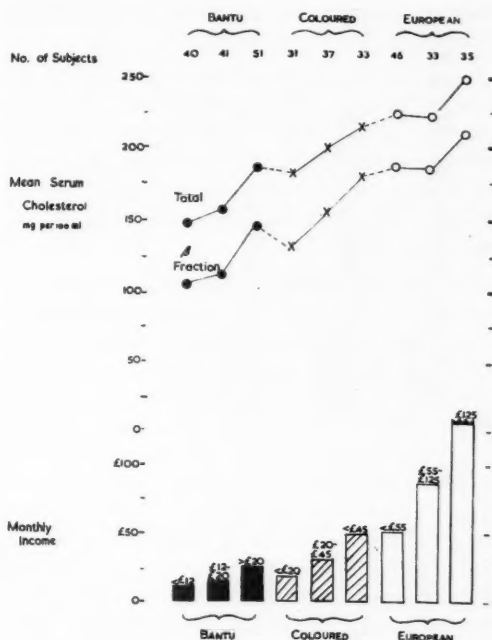


Fig. 1. Mean values for serum total cholesterol and cholesterol content of the beta lipoprotein fraction for the three racial groups each classed according to monthly money income into three sub-groups as follows: Bantu less than 35 dollars, 35 to 55 dollars, over 55 dollars; Coloured less than 55 dollars, 55 to 125 dollars, over 125 dollars; European less than 155 dollars, 155 to 350 dollars, over 350 dollars.

1955) and Bronte-Stewart, Moodie and Brock<sup>30</sup> 1955). In brief, trends that are systematized, i.e., with Bantu at one extreme, European at the other and Cape Coloured in-between, do exist for some of these factors. Some correlate positively with the rise in serum cholesterol and the increase in susceptibility to coronary heart disease from Bantu through Cape Coloured to European. Others show a negative correlation in that there is a systematic decrease in magnitude. A few factors show no systematic trend.

The negative trends are the proportion with elevated erythrocyte sedimentation rates, the proportion classified as heavy manual labourers, the proportion of heavy pipe tobacco smokers and the proportion of non-cigarette smokers. The positive trends are the proportion of sedentary work-

ers, the proportion in employment involving supervisory responsibility, the proportion who are heavy cigarette smokers and the proportion of calories derived from fat. The factors studied that show no systematic trend are alcohol consumption, non-smoking and the degree of obesity as measured by the arm skinfold.

When each ethnic group was subdivided on the basis of income, only two trends remained systematized from low to high income and from Bantu through Cape Coloured to European. These were the degree of supervisory responsibility in the work and the consumption of fat containing foods.

Provided due allowance was made for race and income level there were no significant differences between the mean serum cholesterol levels of individuals with and without elevated erythrocyte sedimentation rates, and of individuals in heavy or light physical labour. The close association between the increase in heavy cigarette smoking and the rising incidence of coronary heart disease (Cuyler Hammond and Horn<sup>31</sup> 1954) was not borne out in our series with respect to the serum cholesterol levels. Nearly twice as many medium income Europeans are heavy smokers as compared with low income Europeans, yet their mean serum cholesterol levels are almost identical. Obesity was as common in the high income Bantu as in the European and in the latter the proportion who were obese was identical in each income group. If these factors do operate in the pathogenesis of coronary heart disease, they must do so through mechanisms other than the serum cholesterol.

Mental stress has often been advanced as a factor in the rising incidence of coronary heart disease though no convincing evidence of this is at hand (Arnott<sup>32</sup> 1954). The greater susceptibility to coronary heart disease of the London bus driver as opposed to the conductor (Morris et al<sup>33</sup> 1953) could as easily be attributed to the greater degree of mental stress as to the lack of physical exertion in the driver. It could explain the susceptibility of the professional and executive occupational classes to coronary heart disease. There is evidence too, that acute emotional stress may shorten the clotting time (Garb<sup>34</sup> 1955). The drop in the incidence of coronary heart disease during the war years in the occupied countries (Strom and Jensen<sup>35</sup> 1951) is often quoted as evidence that prolonged mental strain plays no dominant part. The considerable number of phys-

iological reflexes that come into play in reaction to acute mental stress, are not necessarily exhibited in a reaction to prolonged stress. One of the reactions to acute stress is a rise in blood pressure and another is a rise in serum cholesterol (Kuhl et al<sup>35</sup> 1955). Experimentally it has been shown that only a slight rise in blood pressure or a very labile blood pressure leads to a greater degree of atheroma in rabbits (Bronte-Stewart and Heptinstall<sup>36</sup> 1954) and the hypertension need not be long sustained to produce this effect (Wilens<sup>37</sup> 1943). Furthermore the hypertensive rabbits had slightly higher mean serum cholesterol levels throughout (Heptinstall and Bronte-Stewart<sup>38</sup> 1954). Objective analysis of mental stress as applied in our three racial groups ranging from poverty to wealth is an extremely difficult task. If the lack of any supervisory responsibility at work be taken as a measure, then good correlation emerges with the serum cholesterol levels and our experience of the inter-racial incidence of coronary heart disease.

There remained the diet. The customary Bantu diet, inadequate in certain amino-acids and vitamins carries with it the risk of chronic protein malnutrition with its attendant liver fibrosis, gynecomastia and testicular atrophy. With hormonal theories prominent in coronary heart disease clinical signs of endocrine deficiency were diligently searched for but never found. If birth rate is an index of androgenic activity in the male, perhaps a dubious concept, the Bantu and Cape Coloured are certainly not defective. The customary Bantu diet has yet another link with current problems in the pathogenesis of coronary heart disease. Being deficient in the sulfur-containing amino acids in particular, it provides the Bantu with a dietary protein background not unlike that on which Mann and his co-workers<sup>39</sup> (1953) produced atherosclerosis with cholesterol feeding in the cebus monkey.

Our test for liver disease (Mallen et al<sup>40</sup> 1950) was universally negative, and Walker and Arvidsson<sup>5</sup> (1954) could find no differences in the mean serum cholesterol levels in the presence or absence of liver disease. Calorie excess with its expression in obesity shows no systematized trend.

Batson<sup>41</sup> (1953) had shown that the Europeans consume twice the amount of fat as measured in percentage of total calories derived from fat (35 per cent) as the Bantu (17 per cent). The Cape Coloured lie in-between (25 per cent) (Fig. 2).

Our simultaneous dietary survey, semi-quantitative in that it was assumed that each individual consumed an "average" helping, showed a similar ratio of fat consumption. These marked differ-

ences in fat consumption according to our survey were due primarily to an increased consumption of fat-containing foods of animal origin while the differences between the mean serum total cholesterol levels were due to differences in the cholesterol content of the beta lipoprotein fraction (Fig. 1). When these ethnic groups were subdivided on the basis of income, it became apparent that the more economically privileged consumed greater amounts of animal fat and in many instances this appeared to result from the substitution of animal fat for vegetable fat in cooking methods. Subdivision on the basis of income revealed a striking parallelism between the mean serum cholesterol levels and the animal fat intake.<sup>20</sup> Subgroups on the same economic plane, but of different racial origin, possessing similar mean cholesterol levels, consume similar quantities of ani-

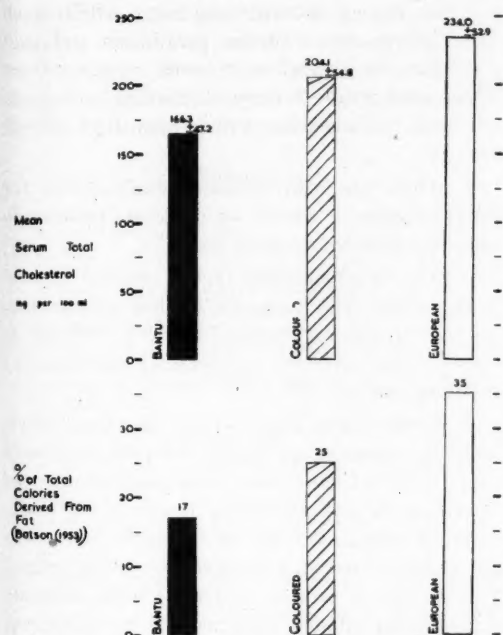


Fig. 2. The relationship between the mean serum total cholesterol of each ethnic group and the percentage of total calories derived from fat.

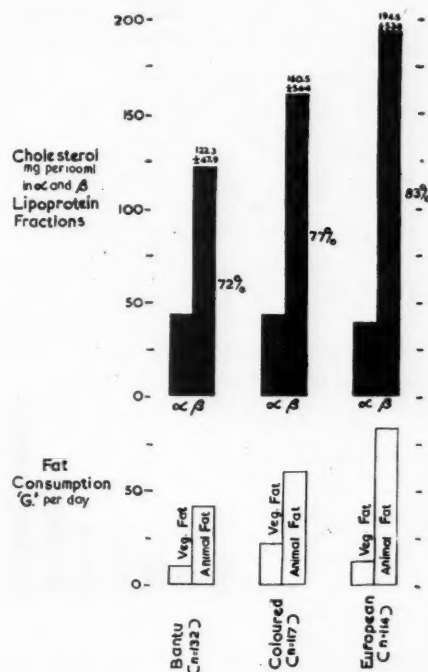


Fig. 3. A rise in the animal fat consumption parallels the rise in the cholesterol concentration of the beta lipoprotein fraction and the mean percentage of the total serum cholesterol located in the beta lipoprotein fraction.

mal fat. Low and middle income Europeans, the former residing in sub-economic housing estates and the latter attempting to ape their higher income counterparts with regard to the stand-

ard of living, consume similar quantities of animal but not vegetable fats. Their mean serum cholesterol levels are almost identical.

In no instance did the mean serum total or beta lipoprotein cholesterol levels correlate well with the vegetable fat intake in this survey. This adds weight to the studies on vegetable fat feeding by Groen et al<sup>42</sup> (1952) and Kinsell<sup>43</sup> (1954), and the studies on true vegetarians by Donath et al<sup>44</sup> (1953) and Hardinge and Stare<sup>45</sup> (1954). It is possible that the conflicting views on this matter (Mayer et al<sup>46</sup> 1954) may have arisen from insufficient attention being paid to the nature of vegetable and fat products and the general pattern of the diet.

The results of our Cape Town survey add weight to the theory that the dietary fat intake influences the level of the serum cholesterol, par-

ticularly that in the beta lipoprotein fraction and in turn may be one of the major factors influencing the pathogenesis of coronary heart disease. This close parallelism offers the greatest

heart disease between these three racial groups is paralleled by (a) mean serum total and  $\beta$  lipoprotein cholesterol (b) total and animal, but not vegetable fat intake in the diet.

4. Comparison of low, medium and high monthly money income subgroups within each racial group shows similar parallelism and suggests that the parallelism between coronary heart disease and serum cholesterol fractions is dependent upon socioeconomic rather than upon genetic factors.

5. There are many possible explanations for the parallelism of trends, which do not necessarily indicate causative associations.

6. The environmental factors related to economic status which justify further examination are (a) stress and strain which is difficult to measure (b) exercise and lack of exercise (c) smoking and (d) diet.

7. In the Cape Town survey the diets which, through economic privilege, are associated with rising levels of blood cholesterol are characterized by rising fat/calorie ratios, due to rising quantities of animal, but not of vegetable, fat. They are characterized also, however, by rising quantities of animal protein foodstuffs with attendant mineral and vitamin patterns and by decreasing quantities of starch and cellulose.

8. The dietary and other environmental factors which are associated with rising mean levels of blood cholesterol and its fractions might determine a rising incidence of coronary heart disease both through the promotion of coronary atherosclerosis and through the promotion of more ready coagulation of blood within the coronary arteries.

### Summary

1. Survey of populations in Africa shows a remarkable freedom of Bantu and Negro from coronary heart disease (myocardial infarction) and from coronary atherosclerosis.

2. These races are by no means free from idiopathic and symptomatic hypertension with its attendant arteriosclerosis (cerebral and renal).

3. The freedom from myocardial infarction is far greater than can be attributed to lower average age and life expectation.

4. It is due in part at least to milder degrees of atherosclerosis of the aorta and coronary arteries.

5. There is no satisfactory evidence that it can

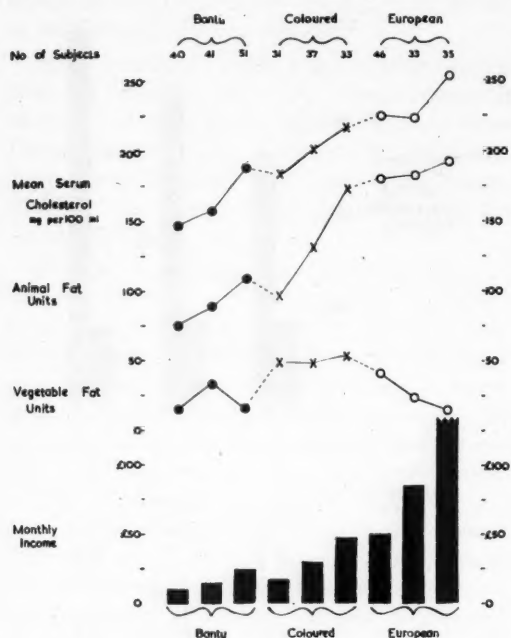


Fig. 4. Mean values for serum total cholesterol and weekly dietary fat intakes (1 fat unit=3.15G (average value) for the three racial groups, each classed according to monthly money income into three sub-groups as follows: *Bantu* less than 35 dollars, 35 to 55 dollars, over 55 dollars; *Cape Coloured* less than 55 dollars, 55 to 125 dollars, over 125 dollars; *European* less than 155 dollars, 155 to 350 dollars, over 350 dollars.

hope that this disease may eventually be controlled and prevented. Certainly there are few problems that merit more attention at the present time.

### Conclusions

1. The results of the Cape Town survey<sup>29</sup> reinforce the conclusions from previous surveys in Africa that the Bantu have a remarkable freedom from coronary atherosclerosis and effects of coronary occlusion.

2. The analyses of electrocardiograms (Vogel-pool and Schrire) shows this freedom to be real for the Bantu in Cape Town. It shows also that the Cape Coloured people are intermediate between the European and the Bantu.

3. The comparative experience of coronary

be attributed to genetic differences in coronary vascular pattern and potential collateral channels.

6. There is some unproven evidence of lesser tendency to intravascular clotting.

7. A controlled interracial study is reported from Cape Town on three racial groups, and tentative conclusions are drawn about the causes of inter- and intra-racial parallelisms between myocardial infarction, serum cholesterol fractions, dietary fat intake and socioeconomic status.

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Little Pamela Schmidt of Minneapolis was born with a gaping hole in the wall separating the pumping chambers of her heart. Apparently normal at birth, Pamela was five months old before doctors discovered her condition—a condition for which there was no known treatment at that time (1950).

For four years, Pamela's mother hoped and prayed for discovery of surgery that would enable her child to live. During the same span, a young team of University research scientists worked hard on a new method of direct-vision surgery within the heart.

Their answer came dramatically on April 23, 1954.

The answer was a donor—a donor whose heart would pump the blood supply for two human beings while the original patient's "dry" heart could be mended. Four-and-one-half hours with her father as the donor, and Pamela was on the road to normal life. Today, she lives the happy life of any other little girl of six.

Six years of heart research produced the successful operation which healed Pamela's heart. Today, a human donor is no longer needed. Further research has produced an oxygenating machine which does the donor's job artificially.

# Treatment of Hypercholesteremia

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THE frequency with which severe hypercholesteremia is associated with atherosclerosis in relatively young ages definitely argues for a causal relationship. It is therefore but natural that many attempts have been made to control hypercholesteremia. Many ways have been tried and

universal therapy, i.e., treatment that will give relief in all cases.

The type of hypercholesteremia regularly seen in untreated myxedema is most likely due to deficiency of the thyroid hormone. It is true that it has not yet been definitely cleared up how hy-

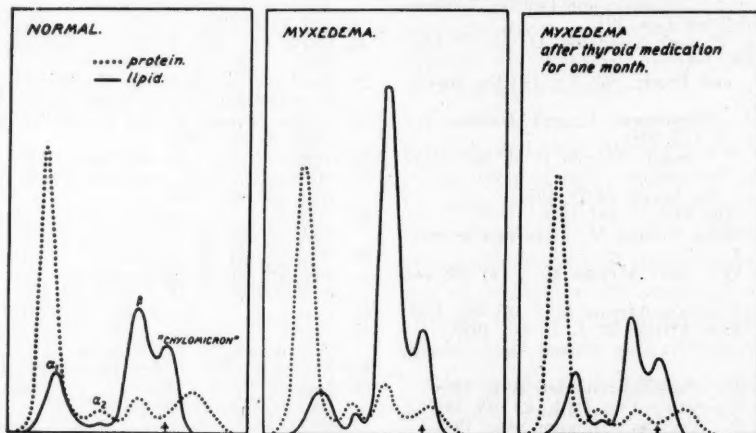


Fig. 1. (left) Electrophoretic pattern of normal serum. The lipids are stained with Sudan black according to the method of Swahn.

Fig. 2. (center) The lipid spectrum in a case of myxedema shows a very high  $\beta$  peak. Total cholesterol 769 mg./100 ml.

Fig. 3. (right) Same case as in Figure 2 after treatment with desiccated thyroid for one month. Total cholesterol: 210 mg./100 ml.

several therapeutic methods based on more or less scientific grounds have been described. Unfortunately, most of these methods have failed to produce anything like reliable results. This is perhaps not so surprising if it be borne in mind that effective treatment of a disease or symptom requires above all clear idea of the cause, and, as far as hypercholesteremia is concerned, our knowledge is still scanty. One thing, however, seems to be certain, and that is that more than one factor is capable of causing hypercholesteremia; therefore we can hardly expect to find a

percholesteremia develops in these cases, but the administration of desiccated thyroid in sufficient doses will bring the serum cholesterol down to normal level within a few weeks. At the same time the blood lipid spectrum will be normalized, a change readily demonstrable by electrophoresis in a filter paper medium by the method of Swahn<sup>1-6</sup> (Figs. 1, 2 and 3). There is a danger in suddenly increasing the metabolism of myxedematous patients who have had angina pectoris or other cardiac symptoms. Several cases of myocardial infarction are on record in which a large initial dose of thyroid preparation had a fatal effect. Therefore, the experienced clinician proceeds carefully and starts the treatment with a very small dose. These fatal cases also provide a

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warning against a less critical use of desiccated thyroid in the management of hypercholesteremia in association with other diseases in which the basal metabolism is not decreased, such as in es-

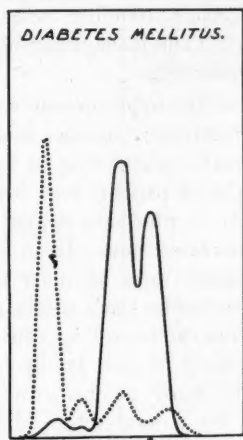


Fig. 4. The lipid spectrum in a case of diabetes mellitus shows a marked increase in both the  $\beta$ -fraction and the "chylomicron"-fraction.

crons" (Fig. 4). The adequate treatment of these cases is to control the disorder of the carbohydrate and fat metabolism by the administration of insulin in sufficient doses. On such treatment the hyperlipemia and the hypercholesteremia usually disappear within a short time. In some cases of diabetes, however, hypercholesteremia persists despite an apparently satisfactory dose of insulin. In these cases the serum is as a rule not creamy. In such patients the hypercholesteremia might have nothing to do with the diabetes but possibly be a manifestation of essential, familial hypercholesteremia.

Creamy serum is also sometimes seen in essential hyperlipemia. Then the neutral fat is markedly increased, an increase accompanied by a pronounced hypercholesteremia. Cutaneous changes are often seen in the form of xanthoma tuberosum—yellow, pea- to nut-sized nodules, most commonly located on the extensor aspects of the elbows and knees, as well as numerous eruptive xanthomata over the buttocks (Figs. 5 and 6). Tendon xanthomata may sometimes occur, though less frequently. Xanthelasma on the



Fig. 5. Xanthoma tuberosum in a case of essential hyperlipemia.



Fig. 6. Eruptive xanthomata over the buttocks in the same case.

sential familial hypercholesteremia, especially if the patient has had myocardial infarction or angina pectoris. Moreover, in these cases thyroid compounds do not produce a very impressive effect on the hypercholesteremia.

As known, hypercholesteremia is fairly common in diabetes, especially in uncontrolled cases with severe ketosis. The serum is then often creamy, which shows that the neutral fat is also markedly increased. The lipid curve shows a high  $\beta$  peak as well as a high peak for the "chylomi-

eylids is also rare. These cases of essential hyperlipemia thus differ distinctly from those of essential familial hypercholesteremia in which the cholesterol deposits are located mainly in the tendons and on the eyelids. Essential hyperlipemia was formerly regarded as a fairly rare disease. Until last year there were only thirty cases on record in the literature. But in a fairly short time we have been able to collect as many as ten cases.<sup>6</sup> Last year Lever and co-workers<sup>7</sup> reported seven cases. Gofman and associates,<sup>8</sup>

likewise in 1954, published lipoprotein analyses of nine cases as well as of twenty-three cases with xanthoma tuberosum, in which ultracentrifugal analysis showed essentially the same lipo-

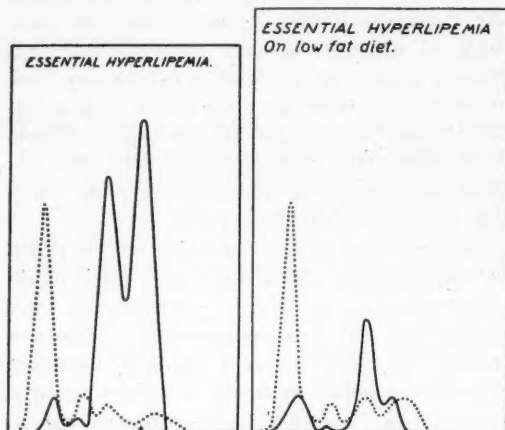


Fig. 7. (left) The lipid spectrum in essential hyperlipemia shows a very high "chylomicron" peak. The  $\beta$ -fraction is also increased.

Fig. 8. (right) Same case as in Figure 7 after treatment with low fat diet.

protein spectrum. Gofman expressed the opinion that patients with xanthoma tuberosum should be assigned to a special group and that only those patients with creamy serum but without cutaneous changes should be classed under the heading of essential hyperlipemia. Personally, we think that this classification is artificial since we have found that of one and the same family, some members had xanthoma tuberosum, while others had a milky serum but not skin lesions. Thus here is an analogy to familiar hypercholesteremia, in which some members of a family have tendon xanthomata, while others have only hypercholesteremia.

Essential hyperlipemia has received increased attention since it has been shown that, contrary to the view of Thannhauser,<sup>9</sup> patients with this condition are by no means spared from atheromatous changes of the arteries.<sup>6</sup> Of our patients six had angina pectoris and three of them had also had myocardial infarction. In such cases a correct diagnosis is of extreme importance, because very effective treatment is available for essential hyperlipemia. This treatment consists simply in the restriction of fat intake to a reasonable minimum. Already within a few weeks of low fat diet the serum becomes clear. The serum cholesterol also drops to normal level, and

if the dietary restriction is strictly observed by the patient for a long time, the cholesterol values and the lipid spectrum will become normal (Figs. 7 and 8). The skin changes can also disappear, and what is particularly encouraging is that the patients can obtain complete relief from their angina pectoris. The management of these cases is thus very rewarding.

Essential familial hypercholesteremia is a common disease, much more common than widely supposed. Systematic examination of the serum cholesterol level in all patients seen because of cardiac infarction or who have angina pectoris will often show increased value. If, in all those cases with a cholesterol value of more than 300, we examine all the brothers and sisters and other relatives for serum cholesterol, we often find distinct hypercholesteremia in one family member after the other. In many of them, the condition is symptomless for a long time. Many, however, have tendon xanthomata, xanthelasma and arcus corneae. Despite the high cholesterol level, the serum is clear and contains a relatively small amount of neutral fat. The most important thing is, of course, that the prognosis of familial hypercholesteremia is very serious because of the regular occurrence of atherosclerosis of the coronary arteries.

The treatment of these cases has been discouraging. A vast number of remedies have been suggested. We have tried choline, inositol and methionine without any definite effect. Heparin and estrogens do not appear to control the serum cholesterol level effectively. On the other hand, Barr<sup>10,11</sup> and others have shown that the administration of estrogens can modify the abnormal lipid spectrum (Figs. 9 and 10). However, when administered in large doses to men, the female sex hormone produces such troublesome side effects that the method can hardly be used routinely.

Sitosterol and other plant sterols will prevent the absorption of dietary cholesterol in chickens and rabbits. We have tried a phytosterol compound (6 gm. per day) in some cases of essential hypercholesteremia, but have in most cases only seen a transient effect on the serum cholesterol.

In 1954, Cottet, Mathivat and Redel<sup>12</sup> described a new compound, sodium-phenyl-ethylacetate, which was said to be able to inhibit the synthesis of cholesterol and thereby to suppress the blood cholesterol level. We have had the

opportunity of trying this compound on some of our patients with hypercholesteremia, but we have not noticed any definite effect (Fig. 11).

Dietary measures have long been tried in the

miliar hypercholesteremia with a diet containing only vegetable fat. Some of the patients in whom the use of vegetable fat was followed by an increase in the serum cholesterol had previously

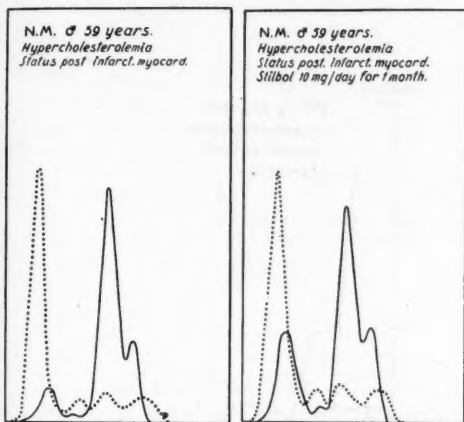


Fig. 9. (left) The lipid spectrum in essential familial hypercholesterolemia shows a high  $\beta$ -peak.

Fig. 10. (right) Same case as in Figure 9 after treatment with oestrogen for one month. The  $\alpha$ -fraction has increased. There is some decrease in the  $\beta$ -fraction.

management of familial hypercholesteremia. Moderate restriction of the fat intake will not produce any impressive effect, but if the patient can live on a practically fat-free diet, such as Kempner's rice-fruit-diet, the blood cholesterol can be reduced considerably. In practice, however, it is difficult to live on such a diet for any length of time. Neither is it sure whether strict observation of such a dietary regime might not with time involve certain risks.

A question that has recently been the subject of much discussion is whether vegetable fat has the same effect on the serum cholesterol level as animal fat. Groen and associates<sup>13</sup> found an exclusively vegetable diet to reduce the blood cholesterol even if the fat content of the diet is fairly high. Kinsell<sup>14-18</sup> has also found that vegetable fat does not increase the cholesterol level but even decreases it. Keys and associates<sup>19-22</sup> and Hildreth<sup>23,24</sup> as well as others, however, are of the opinion that both vegetable fat and animal fat enhance the blood cholesterol. Ahrens,<sup>25</sup> on the other hand, recently came to the same conclusion as Kinsell that vegetable fat decreases the blood cholesterol.

It is difficult to draw any conclusions from these reports about the possibility of treating fa-

been on a low fat diet. Ahrens' series consisted of obese patients who did not have hypercholesteremia. Kinsell's series included one case of familial hypercholesteremia. In that patient the total cholesterol decreased from 420 mg. to 260 mg./100 ml. in the course of the experiment, which lasted thirty days.

During the last few months we have had the opportunity of trying the value of a diet containing abundant vegetable fat in some cases of hypercholesteremia. The vegetable fat was given in the form of artificial milk consisting of corn oil and fat free milk powder, cheese prepared from corn oil, skim-milk and fat free milk powder and ice cream, likewise made of corn oil, milk proteins and sugar. The patients also received bread, cereals, fruits, vegetables, potatoes, rice, spaghetti and sugar ad libitum, although not more than was necessary to fulfill the caloric requirement. Adequate amounts of iron and vitamins were given. In the beginning of our experiments some of the patients also received margarine made from coconut oil and rape oil with no admixture of animal fat.

We tried this vegetable fat diet on different types of hypercholesteremia and also on some cases with normal serum cholesterol. The com-

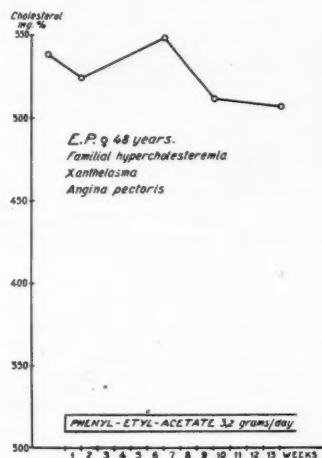


Fig. 11. A case of familial hypercholesteremia treated with phenyl-ethyl-acetate for three months without any obvious effect.

# HYPERCHOLESTEREMIA—MALMROS AND WIGAND

mencement of the vegetable fat die was regularly followed by a distinct fall in the serum cholesterol.

Of special interest are eight cases of hyper-

this regime the ulcer healed in four weeks.\* When placed on the modified ulcer diet, the cholesterol, however, gradually rose again to the previous level. We tried to counteract this increase

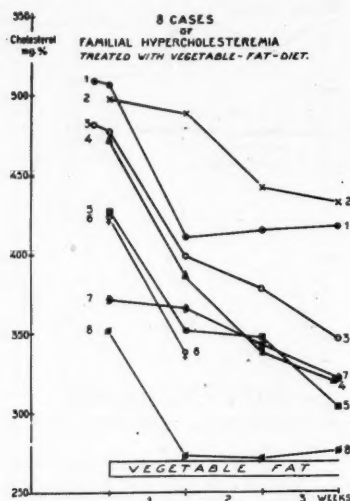


Fig. 12. Eight cases of essential familial hypercholesteremia treated with vegetable fat diet.

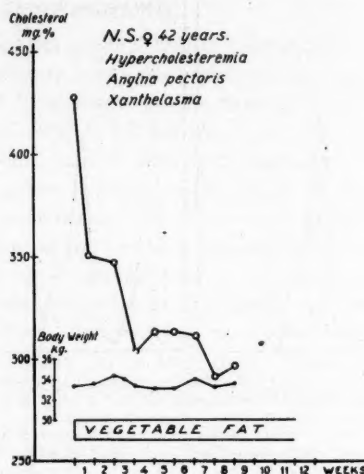


Fig. 13. A case of essential hypercholesteremia treated with vegetable fat diet for two months.

cholesteremia of the essential, familial type, as such cases do not respond very well to other therapy. Four of them belonged to one and the same family. Two had tendon xanthomata, six had angina pectoris and of these, four had had myocardial infarction. As shown in Figures 12 and 13, the cholesterol fell abruptly, when animal fat was replaced by vegetable fat. Most of the patients have not yet been on the diet for more than a few weeks. It being known from similar experiments with low fat diet that the serum cholesterol often increases after a temporary decrease, the trial will be continued for a long time.

One of the patients had fairly severe gastric distress during the test period. The patient thought it might have something to do with the corn oil "milk," although the flavor of this preparation was not disagreeable. It turned out, however, that he had a peptic ulcer. Gratifying the desire of the patient we then changed the diet. He received a modified ulcer diet in which part of the corn oil "milk" was replaced by vegetable margarine. He still received no animal fat. On

by administration of a phytosterol compound but it had only a transient effect on the serum cholesterol (Fig. 14).

It is, of course, not possible from this single experiment to say whether the rebound of the serum cholesterol to the previous level had anything to do with the change in the diet or whether it was spontaneous. However, in some other cases we also observed a similar effect, i.e., when vegetable margarine was added to the diet or when it was used instead of corn oil, the serum cholesterol increased. For that reason we have recently eliminated margarine from the diet and use nothing but corn oil.\*\*

These observations suggest that not all kinds of vegetable fat produce the same effect on the serum cholesterol. This might also help to explain

\*Later on we tried a modified ulcer diet including abundant corn oil "milk" in other cases of peptic ulcer with satisfactory results. The ulcers have healed in three to four weeks.

\*\*Some weeks ago, when Ahrens<sup>26</sup> visited Lund, he told us that investigations at the Rockefeller Institute in New York had shown that coconut fat does not produce the same decrease in serum cholesterol as corn oil.

some of the apparently contradictory results obtained by various workers in this field.

Many different factors may influence the cholesterol metabolism; it is therefore important that

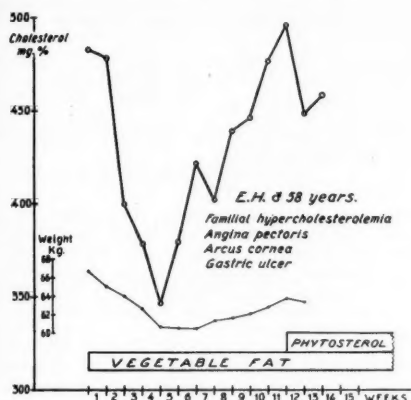


Fig. 14. A case of familial hypercholesterolemia treated with vegetable fat for three months. When a gastric ulcer was discovered after one month the diet was changed to a modified ulcer diet in which part of the corn oil "milk" was replaced by vegetable margarine. He still received no animal fat. The serum cholesterol curve rose again in the next two months to the previous level.

the experiments are kept as clear cut as possible in clinical investigations of this type. Wilkinson, Boyle, Jackson and Benjamin<sup>27</sup> have shown that a preceding period with low fat diet can influence the results of a later high vegetable fat diet. This is also evident from one of our cases of essential hyperlipemia (Fig. 15).

This patient had been on a low fat diet for years during which his earlier creamy serum had become clear and the cholesterol values normalized. But when we placed him on a high vegetable fat diet the serum again turned creamy and the cholesterol values increased. We stopped the trial and again placed him on a low fat diet. The patient was then sent home. However, some time later he got tired of the low fat diet and began to eat ordinary food including butter, eggs and other animal fat in fairly large amounts. Already within a few weeks the serum was creamy and the cholesterol values had risen to 640 mg./100 ml. The patient was again placed on a vegetable fat diet and this time the response was different: although the serum was still milky, the cholesterol decreased.

The way in which vegetable fat influences the cholesterol metabolism is not known. It is hardly

the absence of cholesterol in the vegetable fat that is of decisive importance. The favorable results obtained with corn oil might possibly be due to the abundance of essential fatty acids in

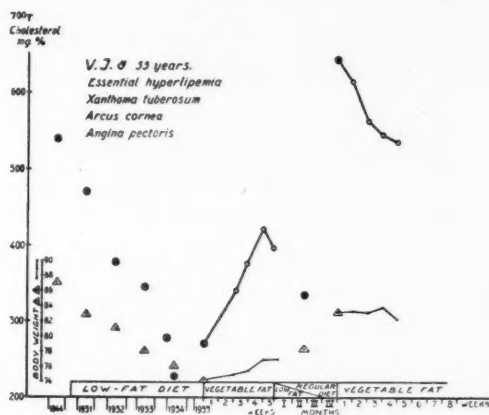


Fig. 15. A case of essential hyperlipemia successfully treated for several years with low fat diet. When the diet was changed to a high vegetable fat diet the cholesterol rose again. After a period of regular mixed food containing much animal fat a diet high in vegetable fat resulted in a fall of the serum cholesterol.

this kind of fat. As much as 57 per cent of corn oil consists of linoleic acid. According to Holman,<sup>28</sup> the essential fatty acids play an important rôle in the transport of cholesterol. The effect of various fatty acids on the level of the blood cholesterol and on the development of arteriosclerotic changes in the arteries constitutes a particularly important field for future work.

### Acknowledgments

It is a pleasure to acknowledge the contribution of Dr. Bengt Swahn to these investigations. The series could not have been collected without the kind co-operation of Professor J. Waldenström, Malmö, and Dr. G. Myhrman, Örebro. We are very grateful to Docent Bengt Borgström for valuable suggestions and advice concerning the vegetable fat diet and inspiring discussions. Acknowledgment is due to Dr. G. Wode, Stockholm, for supplies of corn oil, and to Professor P. Swartling, Alnarp, and his staff for preparing the artificial milk and cheese. We are indebted to Miss K. Sonesson and Miss Hanna Nilsson for the preparation of the vegetable fat diet and to Miss I. Kockum for technical assistance.

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## DISCUSSION—ARTERIOSCLEROSIS OF THE EXTREMITIES

(Continued from Page 835)

arterioles will show a decreased pulse volume on warming of the entire body to create vasodilatation and in a cold environment upon the use of vasodilating agents. Furthermore, some of these individuals who have had and are helped by sympathectomy in a cold environment experience this same pulse volume diminution on whole body vasodilatation by heat or priscoline.

It is reasonable to say that we should be discriminating in prescribing vasodilating drugs to arteriosclerotic individuals and in particular we should abandon this use in those patients who have undergone sympathectomy. For the same reasons we should probably abandon the use of an exceptionally warm environment for these same patients after a sudden occlusion.

Another interesting finding was made in experiments conducted on rabbits by my colleague, Dr. Thomas Murphy. Rabbits on an atherogenic diet were found to de-

velop marked atherosclerosis of the entire aorta down to and including the renal arteries. A similar group of animals subjected to bilateral lumbar sympathectomy developed a more extensive atherosclerosis involving the distal iliac and femoral vessels. Little or no atherosclerosis was found in the group of animals on a normal diet with or without sympathectomy.

The examination of the long range effect of sympathectomy is obviously a difficult one to accomplish. It is remotely possible that sympathectomy may enhance atherosclerosis of the larger vessels in atherosclerotic patients as it was found to do in the rabbit while it opens the arterioles and other collaterals. This does not contraindicate sympathectomy in individuals where a vasomotor component is repeatedly depriving the extremity of its nourishment. But it does make one reconsider the advisability of sympathectomy in the extremity with a questionably detrimental vasomotor component.

# Electrocardiogram in Coronary Heart Disease

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THERE is no type of electrocardiographic abnormality which has not been observed in coronary heart disease, and the accumulated literature is enormous. But it is not my present purpose to review the present state of the various aspects, problems, and approaches. I propose here

members of the Minnesota population (Lober),<sup>2 a, b</sup> so that at least in geographical respect the groups are comparable.

Table I shows, in column 1, the difference in relative coronary artery lumen (which is one of the best criteria of arteriosclerotic degeneration)

TABLE I.

Coronary artery lumen (per cent of artery area) in 21 cardiovascular normal young (Y) and 20 older Minnesota (O) men, and selected ECG items in 47 young and 52 older men in Minnesota and in Italy. M=means; SD=standard deviations; ..=mean difference between age groups and their statistical significance=t.

	Coron.* Lumen %	Minnesota			Italy**		
		ST mm	Axis° QRS	Axis° T	ST mm	Axis° QRS	Axis° T
Y M	44.52	7.46	68.87	44.85	5.35	42.83	35.04
SD	7.88	2.01	17.44	19.92	2.70	30.76	20.86
O M	31.50	5.16	45.19	26.65	4.94	35.56	34.85
SD	8.10	1.67	29.97	23.66	2.15	26.10	21.77
..	-13.02	-2.29	-23.68	-18.19	-0.41	-7.27	-0.19
t	5.2**	6.2**	4.7**	4.2**	0.8	1.3	0.04
Per cent change	-29.3	-30.9	—	—	-7.6	—	—

\*P Lober

\*\*A. Keys

to discuss the broad problem of the differentiation of normal from abnormal, a question which has received comparatively little attention in general and, in regard to electrocardiography, in particular.

A progressive development of coronary sclerosis is one of the most impressive normal biological age trends in man. Allowance for the effect of this on the electrocardiogram appears to be essential for the interpretation of electrocardiogram in coronary heart disease.

Statistically highly significant differences in most electrographic (ECG) items were found when a group of 157 normal young men was compared with a group of 233 middle-aged men in Minnesota.<sup>1</sup> Fortunately, one of the most detailed autopsy studies on arteriosclerotic changes in 536 hearts was made, independently, on mem-

bers of twenty-one younger and twenty older men who died from trauma or acute illness. This is compared with the age difference of a few selected ECG items between forty-seven young and fifty-two older men in Minnesota (columns 2-4) and in Italy\* (columns 5-7). Both ECG groups were randomly selected but matched as to number, body weight distribution and mean age.

Table I shows a definite parallelism between relative coronary artery lumen and ECG changes in the Minnesota men. The Italians, however, do not show these ECG changes with age. This seems to be highly suggestive of a causal relationship because the incidence of advanced coronary sclerosis and of coronary heart disease is much lower in Italy. It seems to be a reasonable hypothesis, at least meriting more extensive study, that such ECG age trends as we see in Minnesota are, in fact expressions of progressive coronary atherosclerosis. This would mean, among

\*Recently collected by Dr. A. Keys.

From the Laboratory of Physiological Hygiene, University of Minnesota Medical School, Minneapolis.

Presented in the Symposium on Arteriosclerosis, University of Minnesota, Minneapolis, September 9, 1955.

other things, that the ECG might provide a useful estimate of the incidence of coronary sclerosis in the general population, but, of course, not necessarily for the individual.

ble in patients with coronary heart disease than in normal persons is common clinical experience, but no precise information was available.

The intraindividual standard deviation was de-

TABLE II.

Means (M) and Standard Deviations (S. D.) of selected ECG items in 15 patients (P) with angina pectoris and normal resting ECG, compared to 233 normal older men (O)

Group		R <sub>2</sub> mm	T <sub>1</sub> mm	T <sub>2</sub> mm	ST mm	QRS axis°	T axis°	T-V <sub>4</sub> mm
P	M	7.05	1.71	1.46	3.93	11.00	16.67	3.61
	S.D.	3.79	0.87	0.77	1.35	29.86	33.13	2.24
O	M	7.75	2.01	2.26	5.20	37.77	32.87	7.08
	S.D.	3.16	0.89	0.95	1.74	34.67	23.96	2.49
	t	-0.70	-0.30	-0.80	-1.33	-26.77	-16.20	-3.47
	P	0.82	1.27	3.19	2.77	2.92	2.54	1.71
	P	0.42	0.21	0.002	0.006	0.005	0.015	0.09

Many people with advanced coronary sclerosis do not develop coronary heart disease, but all who do so have extensive and advanced arteriosclerotic degeneration. If clinical coronary heart disease can be considered as the extreme result of a process related to age a gradual transition rather than a sharp separation between the so-called normal population and patients should be expected. This is actually the case. In a high percentage of patients with typical angina pectoris, the ECG is within the normal range limits as customarily defined.

Although the ECG of an individual patient with coronary heart disease may be "normal," significant group differences between such patients and the normal population do exist, as we have found. We compared selected items in the resting ECG of 233 older clinically healthy men and in fifteen angina pectoris patients whose electrocardiograms in rest were normal but became abnormal after exercise (Table II).

All changes in the group of patients are in the direction of average age trends we find in clinically healthy men in Minnesota and they are statistically highly significant in four of the seven items studied. In another item (T-V<sub>4</sub>), the difference approaches statistical significance. The results show that the ECG is affected already in the initial phase of coronary disease though the changes are not sufficient to move the ECG of many individual patients clearly outside the wide normal range limits. The results correspond to the concept of a gradual transition from normal age trends to coronary heart disease.

We have approached this problem from still another angle, that is the variability of the ECG in repetitions. That the ECG is more varia-

terminated from repetitions after six weeks with fifteen coronary patients whose electrocardiograms were normal in rest and with thirty coronary patients with abnormal electrocardiograms in rest; these represent earlier and a more advanced phase of the disease (Table III). Patients with acute episodes of severe coronary insufficiency of myocardial infarct were not included. For comparison, data on the annual repeat variability of 100 older men was available. The intervals between repetitions are not identical, but if anything, the longer interval of the normal group should be expected to result in larger variability. In all items except ST the repeat variability in the patients with abnormal resting ECGs is significantly higher than in the "healthy" men. The repeat variability of the T axis in these patients is enormous. Coronary heart disease, therefore, increases significantly the repeat variability as the ECG becomes abnormal. The repeat variability of the coronary patients with normal ECG is significantly increased only in the T-axis, which seems to precede the development of frank abnormalities in the electrocardiogram.

This finding may have potential diagnostic interest, and in any case it conforms to the concept of a gradual transition from normal age trends to the picture of frank coronary heart disease.

Wide overlapping of normal and abnormal distribution was recently demonstrated for Q<sub>3</sub> and twenty-two related ECG items even in such an advanced stage of coronary heart disease as posterior wall myocardial infarct.<sup>8</sup>

In this situation, various stress situations such as exercise, anoxia, meal intake, and drug effects

## ELECTROCARDIOGRAM IN CORONARY HEART DISEASE—SIMONSON

have been used with advantage for detection of coronary heart disease. All of these tests produce an abnormal ECG response in an appreciable number of patients with angina pectoris whose

cently obtained for two types of exercise (treadmill walking and step test) in our laboratory.<sup>5</sup>

All ECG stress tests have been developed primarily for detection of latent coronary disease,

TABLE III.

Six-week variability (S.D.) ECG items in patients with coronary heart disease and normal (Cor. N) and abnormal (Cor. A.) ECG, compared to annual variability in older normal men (N). Statistical significance shown by F test.

Group	No.	P-R int. 1/100 sec.	T <sub>1</sub> mm	Tv <sub>1</sub> mm	SQRS mm	ST mm	QRS Axis°	T- Axis°
N	100	11	0.54	1.66	2.47	1.12	8.44	10.29
Cor. N	15	13	0.38	2.13	2.38	0.92	10.94	26.29
Cor. A	30	26	0.73	2.69	4.99	1.03	13.13	63.98
F	—	N.S	N.S	N.S	N.S	N.S	N.S	6.52**
N	—	—	—	—	—	—	—	—
Cor. A	—	5.59**	1.82*	2.63**	4.07**	N.S	2.42**	38.62**
F	—	—	—	—	—	—	—	—
N	—	—	—	—	—	—	—	—
Cor. A	—	4.00**	3.75**	1.60	4.41**	N.S	1.44	5.92**
F	—	—	—	—	—	—	—	—

electrocardiograms are normal in rest but there is wide disagreement as to the percentage of abnormal responses produced by the various stresses. This is due to the lack of independent objective criteria to define latent coronary disease, and because different electrocardiographic criteria have been used for differentiation between normal and abnormal responses.

A considerable overlap should be expected also in the distribution of "normal" and "abnormal" responses when clinically healthy subjects are compared with patients. Actually, this is precisely what is found in spite of highly optimistic claims for this or that test as a means of detecting coronary heart disease. Master<sup>4</sup> has claimed a 95 per cent diagnostic accuracy for his two-step exercise test but this is certainly misleading. Such a high percentage of "positives" among patients with coronary heart disease can only be achieved at the expense of including a very large number of false positives among the clinically healthy population.

In our own studies normal range limits for conventional and vectorial ECG items were re-

but "abnormal" responses are also obtained in other cardiac and non-cardiac diseases. However, no large groups of patients with diseases other than coronary heart disease have been studied, and therefore we cannot tell with certainty how much more specific an abnormal exercise test would be for coronary heart disease than for other types of pathology.

Further work in these directions, using the conventional as well as the newer vectocardiographic methods, appears to be promising.

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The Minnesota Heart Association raised a record \$379,000 in the 1955 Heart Fund campaign. Hennepin County produced \$161,063 of the total. Generosity and genuine concern of Minnesotans regarding the heart disease problem is reflected by their 1955 performance. Minnesota ranks eighteenth in population, yet only seven other states raised more than Minnesota in the Heart

Fund drive in 1955. Goal in the state for the February, 1956, drive is \$380,000. State chairman will be E. B. Eliason, Jr., of Minneapolis. Approximately 30,000 volunteers will undertake the drive in Minnesota come February 1. Despite past successes, Mr. Eliason says, MHA was able to supply only half the research funds requested by state projects in 1955.

# Quantitative Electrocardiography

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RATHER than attempt a detailed discussion of Dr. Simonson's excellent work, I thought I would discuss how advances may be made in the quantitative interpretation of the electrocardiogram, using a few examples from the literature and some from our own recent attempts.

The process which is essential and final for the physicist, physiologist, or physician dealing with electrocardiographic wave forms, no matter how obtained or how recorded, is the interpretation of the record. The process of interpretation of electrocardiograms by the physician has for many years been essentially unchanged.

Interpretation of the electrocardiogram has consisted of making a few quantitative measurements such as the PR, QRS, and QT intervals, and then describing in qualitative or correlative language the size and shape of the deflections. Qualitative descriptive words such as "low," "high," "sagging," "peaked," and "depressed" are frequently used; or, correlative words such as "strain," "coronary type," and "digitalis type" are also frequently used. The mental process of the interpreter of the electrocardiogram is remarkable. It involves a visual estimate of the size and shape of the electrocardiographic waves in many leads, an estimate of the size, shape, and direction of the QRS relative to those of the T waves, and finally a comparative estimate with the limits of normal variations of these estimates and with the various patterns of abnormal variations. This is a fairly complicated process. Most of this interpretive process is not quantitative, nor is it expressed in values which can easily be compared, reproduced, or communicated to other interpreters.

Dr. Simonson has properly emphasized that one of the most difficult parts of the process of interpretation is to define the limits of normal

variation and to separate clearly the normal from the abnormal. In addition, there is the problem of expressing degrees of abnormality. The final step is to correlate the changes in the electrocardiogram with other pieces of evidence obtained from the historical facts and physical examination, and from histological, pathological and physiological chemical observations. The interpretation of the electrocardiogram in the last step can only be an accurate predictive diagnosis if there is previous correlative experience of an accurate clinical, pathological, or physiological nature. In other words, for clinical purposes, the electrocardiogram is only as accurately diagnostic as the information with which it has been previously correlated.

Aside from research which correlates the electrocardiographic picture with disease, drugs, stress, or physiological findings, there are two other approaches to electrocardiographic research which have had some recent bearing on the process of electrocardiographic interpretation. I have divided electrocardiography into three categories of study, the first of which has been mentioned, namely, *correlative or diagnostic electrocardiography*. The second category might be termed *analytic electrocardiography*. In this category are the endeavors of research workers to map the electrical field in and on the surface of the body, and to study the factors influencing the conduction of the generator signals through the medium of the body.

The third type of research might be *synthetic electrocardiography*. In this category are the attempts to put into a more unified picture the pieces of the electrical forces of the heart obtained from isolated leads or reference points. Most of the attempts to do this have been based on the general assumption (or hope) that the heart acts essentially as a point source or generator in the center of an electrically homogeneous conducting medium, namely, the body. This is the basis for the use of the vector method for representing the electrical information from the

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Presented in the Symposium on Arteriosclerosis, University of Minnesota, Minneapolis, September 9, 1955.

heart. The vector theory is a unifying concept of the heart's electrical activity. All the known clinically useful information about the heart's electrical activity should be contained in the vector figure. It should be possible to find three bipolar reference leads representing all the electrical information in the three planes of the body. It should also be possible then to derive any local or special surface electrocardiographic view one desires from a primary electrocardiographic information obtained at a distance.

A good deal of experience with the technique based on the vector theory shows that practically all the electrocardiographic information which we obtain by applying leads at multiple points on the surface of the body, particularly on the chest, can be derived from recordings from distant reference axes. Between the observations of Milnor and ourselves, we have examined over a thousand subjects with all sorts of abnormalities. We have yet to find information which is of any use for clinical correlation or interpretation in the electrocardiograms obtained from multiple surface leads which cannot be derived from three simple bipolar electrocardiographic leads taken at a distance representing the electrical information in the three axes of the body.

The question arises: What does one consider clinically significant information? At the moment, we can only state that physicians who have had ten to fifteen years' experience in heart stations reading twenty to forty electrocardiograms per day can find no more diagnostic information in the conventional twelve lead electrocardiogram than can be obtained by separate independent interpretation of the distant three vector reference lead electrocardiograms recorded simultaneously.

An example of this technique is shown in Figure 1. Above are the electrocardiograms as recorded by conventional techniques using the V leads across the chest. Below are the electrocardiograms which were derived or calculated by an electronic instrument, from the three electrocardiograms recorded from distant leads on the body. You can see that the information which is diagnostic, and which has been perhaps in the past thought to be rather special local or semi-direct information, is contained in distant leads which are nowhere near the usual locations of the chest leads. These electrocardiograms are

obtained by a synthetic calculating process from three leads formed from a total of four electrodes placed on the back and near the right shoulder, with only one electrode on the front of the chest.

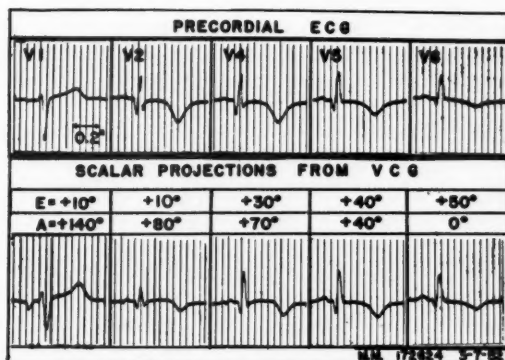


Fig. 1. Illustration from the work of Milnor et al. Above are the actual precordial electrocardiograms from a patient with an anterior myocardial infarction. Below are the electrocardiograms derived with a Schmitt instrument (variously called a "resolver," a "panoramic unit" or a "vector aspect changer"). The primary information from which the leads are derived consist of three bipolar leads placed according to Milnor's system. E is the elevation and A the azimuth in degrees of the reference line of the projections (see Figs. 2 and 3). This demonstrates the practical validity of the vector concept of electrocardiography, and encourages us to proceed upon the assumption that all the useful clinical information is contained in three bipolar leads properly placed at a distance from the heart. Conversely, it means that there is practically no special or "semi-direct" information in multiple leads on the chest anatomically closer to the heart.

The questions arise: What is the use of this different set of leads? What sort of advance is this? The value of this demonstration is that it allows us to think of the electrocardiographic picture from the total integrated viewpoint rather than from the viewpoint of each lead giving us some special isolated underlying information. It reduces the electrocardiogram from twelve leads to three. Secondly, this method may lead us to more quantitative expressions of interpretative correlative data. As an example of what is meant by this, let us consider the problem of the significance of the presence of a Q wave in standard Lead III of an electrocardiogram (Fig. 2). The vector force which creates a  $Q_3$  points upward in the frontal plane away from the foot. However, when this initial " $Q_3$ " vector is viewed from the side of the body rather than from the front of the body, we find that in the normal subject it points forward and upward. In patients who

have been judged to have had a posterior myocardial infarction from other definite clinical criteria, we find that the "Q<sub>s</sub>" vector points directly upward and frequently backward (Fig.

the height. However, if the information is correlated with the movement of the vector in another direction, more quantitative reproducible information can be obtained and we can assign

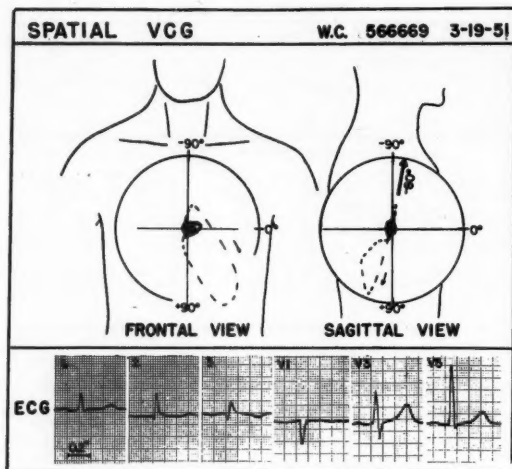


Fig. 2. This shows the vector cardiographic tracing in a patient with posterior myocardial infarction (from Milnor et al), and the scalar electrocardiographic leads. The initial 0.04 vector which results in a Q<sub>s</sub> deflections, points toward the head and to the left.

3). As more data is accumulated, some normal subjects and some patients with myocardial infarction may have initial 0.04 vectors in the sagittal view which point in the same direction. This again leads to difficulty in interpretation. However, the method is helpful because the limits of normal can be quantitatively defined. One would like to have a completely accurate diagnostic tool, but I am afraid the instrument or the method of interpretation will not alone resolve all problems. All we can hope to do is sharpen the differences between the normal and abnormal. If we can express these things in quantitative terms, we have a chance for more accurate interpretation. The fact that the Q<sub>s</sub> wave or the initial 0.04 vector tends to point upward and backward in posterior myocardial infarction is another expression of the fact that in posterior myocardial infarctions the R waves of the initial 0.04 vector in the anterior chest leads; that is, V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> tend to be low or absent. The difficulty in interpreting the height of the R waves in V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub>, however, is one of quantitation. It is very difficult to visually and mentally estimate

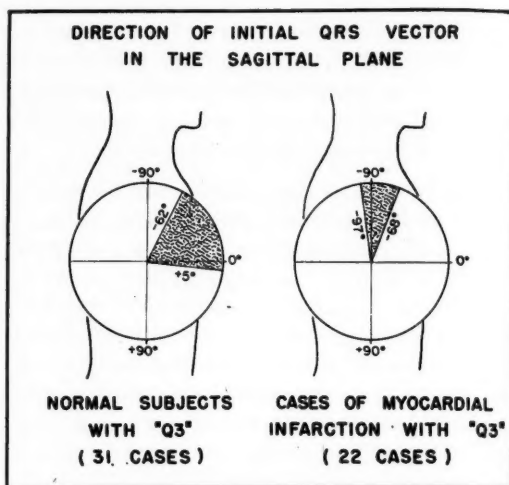


Fig. 3. An analysis of direction of the initial 0.04 vector in normal subjects and cases with posterior myocardial infarction with Q<sub>s</sub> deflections. The best quantitative differentiation of the normal from the abnormal is obtained by the vector addition of forces in all directions (from Milnor et al), obtained from a simple bipolar three lead system representing the electrical forces in the three planes of the body.

not only a size but an accurate direction in space to the potential.

There is another concept of vector additions which may be useful. A long time ago, Wilson injected some quantitative ideas into the interpretation of the electrocardiogram when he introduced the concept of ventricular gradient. Ventricular gradient is an attempt at quantitative expression of the mental process mentioned previously, namely, the process of making an estimate of the size and direction of the QRS deflection relative to those of the T wave of each lead. Dr. Johnston was one of the first, in 1950, to report an attempt to facilitate the process of determining the areas under QRS and T waves by using electronic circuitry. Recently, in our laboratories, Thomas Arnold and Dr. James McGovern have made advances in instrumentation which will facilitate quantitative analysis of the areas of the QRS and T waves.

We have combined the unifying concept of the vector method with the idea that comparison

of the areas of the QRS and T waves is fundamentally important in interpretation. If all the known clinically useful information about the heart's electrical activity is contained in three

vector integral electrocardiogram. Integrating circuits were devised which would deliver a voltage proportional to the area accumulated under each QRS T complex. An example of this

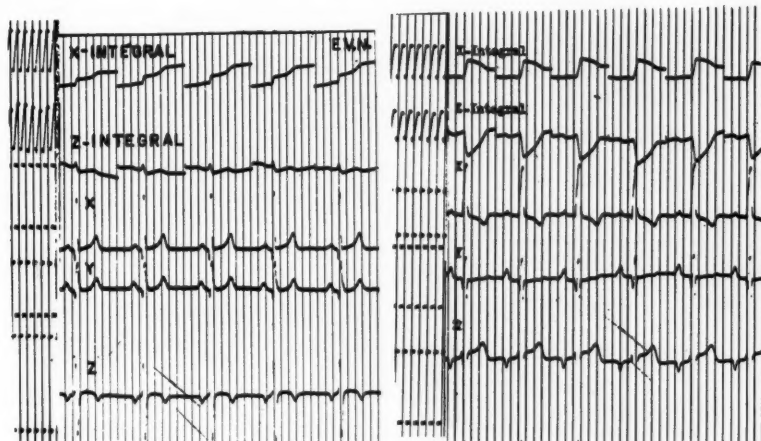


Fig. 4. (left) The three normal scalar electrocardiograms and two scalar simultaneous integrals. The X, Y, Z leads are bipolar. The X lead is formed by electrodes on the back in the mid-clavicular lines directly opposite the second anterior interspaces on both sides. The Y lead is between the right back electrode above mentioned and an electrode placed directly below at a distance equal to that between the two X lead electrodes. The Z lead is formed by placing an electrode on the right anterior chest directly opposite the right upper back electrode. The positive sense of both the electrocardiogram and integral deflections is toward the patient's left, front, and foot.

The calibration deflections represent 1.0 millivolt input for the electrocardiograms and 0.05 second millivolt input for the integrals. Each cycle is integrated separately beginning and ending the integration in the T-P interval. (The variation of the calibration signal the Z integral channel was due to temporary instability of the signal generator.) Time lines are 0.10 seconds.

Fig. 5. (right) The X Y Z scalar electrocardiograms and the X and Z simultaneous scalar integrals in a patient with left ventricular hypertrophy due to aortic stenosis. Technique and calibrations same as for Figure 4.

bipolar reference leads, it should be possible to obtain a three-dimensional unified concept of the relative areas. The hope is that this synthesis of information would dissolve the differences between normal people, and sharpen the differences between the abnormal patterns and the normal.

Many of the differences in electrocardiographic patterns are "positional," and at the present stage of our knowledge it would be difficult to say which electrical view of the heart is the "correct" one. The correct view from the practical clinical standpoint is the one which gives the most reliable differentiation of disease. Utilizing the vector concepts and area measurements, and encouraged by Schmitt on the validity of vector leads, we have proceeded to develop electronic methods for the vector addition of area measurements. This procedure might be called the three dimensional

continuous process is shown in Figure 4 for a normal person. The scalar electrocardiograms are called X, Y, and Z representing respectively the electrical forces in the side-to-side, up-down, and front-back directions of the body. The continuous simultaneous integrals of each cycle are recorded for the X and Z co-ordinates. These two co-ordinates form the transverse plane. The same process is shown in Figure 5 for a patient with left ventricular hypertrophy. When the integration for each cardiac cycle is completed, the integration starts for the successive cycles at the new baseline.

The continuous accumulation of area in two directions can now be added vectorwise continuously, using an oscilloscope. Illustrations of the vector additions of the scalar electrocardiograms and the scalar integrals are presented for

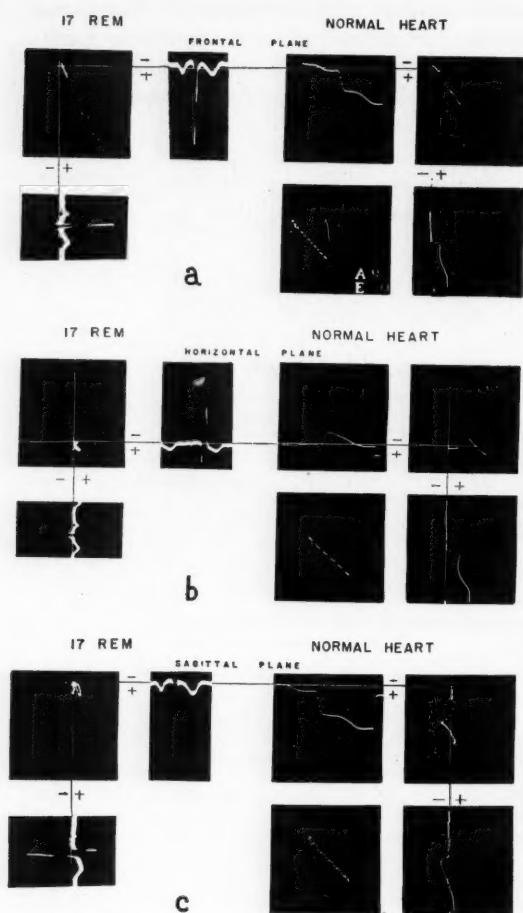


Fig. 6. (a) A composite chart showing, in a normal subject, the frontal plane vectorcardiogram (VCG) (top left) and the frontal plane vector integral cardiogram (VICG) (top right) with the scalar components of each arranged in their spatial relations. Calibration signal included which produces the line at  $45^\circ$  to both axes.

Time markings are made in the VCG and VICG, and on the scalar integrals by interrupting the beam. Thus, during the rapid accumulation of area during the QRS, the dots are farther apart, while during the slower T wave area accumulation, the dots tend to fuse.

(b) The normal horizontal plane vectorcardiogram and vector integral cardiogram with the scalar components of each.

(c) The normal sagittal plane vectorcardiogram and vector integral cardiogram with their scalar components.

a normal subject in Figures 6a, 6b, and 6c, and for a subject with left ventricular hypertrophy in Figures 7a, 7b, and 7c, in the three planes of the body.

### Summary

I have limited my comments to possible ways

to make advances in the process of quantitative electrocardiographic interpretation. The process of electrocardiographic interpretation has been too seldom a quantitative one. The progress in validation of the vector theory of the heart's electrical activity has helped somewhat to free us from isolated viewpoints of electrocardiographic leads. Some of the vector additions of electrical information may help in separating the normal from the abnormal, and describing the degrees of abnormality. The concept of ventricular gradient which is another type of vec-

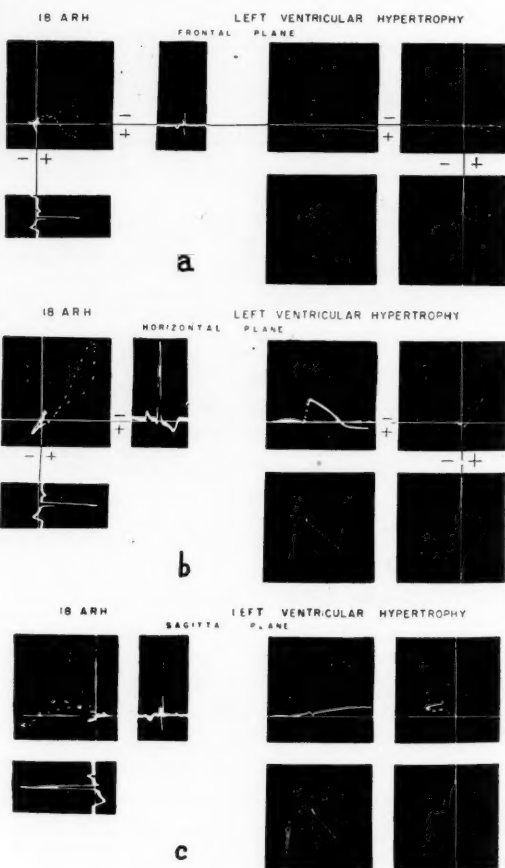


Fig. 7. (a) A composite chart showing, in a patient with left ventricular hypertrophy due to aortic stenosis, the frontal plane vectorcardiogram (VCG) and the frontal plane vector integral cardiogram (VICG) with their scalar components.

(b) An abnormal horizontal plane VCG and VICG with scalar components in a patient with aortic stenosis.

(c) The VCG and VICG with their scalar components in a patient with left ventricular hypertrophy.

tor addition has always been important in interpretation, and I believe new methods now make it possible to further test and extend the value of this concept of quantitation in the future. By utilizing a simple three lead system and continuous integration with vector addition, a three dimensional vector integral electrocardiogram (VICG) may be obtained. The value of this method of representation remains to be proved, but it is now possible to proceed with the facility and accuracy of automatic computation. Finally, even though we can quantitatively represent the electrocardiograms, none of the quantities will be useful unless they are correlated carefully with equally accurate quantitative information obtained from clinical facts, from pathological and histological examination, and from physiological and chemical observations.

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## ANEURYSM OF THE ABDOMINAL AORTA

(Continued from Page 838)

are present. It also will show the relationship of the area of obstruction to the renal and mesenteric arteries and will give some information of value concerning collateral circulation. As is the case in aneurysm of the aorta the aortogram does not always reveal correctly all details of the true situation, and if from the appearance of the aortogram there is uncertainty as to operability of the lesion, an abdominal exploration may be justified.

The two points of the clinical evaluation of occlusion of the abdominal aorta which are of greatest importance when treatment is being considered are: first, to determine by a careful history how much the symptom of intermittent claudication is really impairing the usefulness and happiness of the patient, and secondly, to determine, if possible, by examination whether or not any of the large arteries distal to the bifurcation of the aorta are occluded.

As more experience is gained with this condition and knowledge concerning arteriosclerosis in general increases, we physicians will be better able to evaluate the degree of arterial vascular disease in the lower part of the body and particularly in the extremities of these patients, and to evaluate the probable future complications and the hazards to life and limb if the condition is untreated. Then we can apply this clinical knowledge with more certainty than is possible at present in advising our patients as to the best method of treatment.

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## Ballistocardiogram in the Diagnosis of Coronary Atherosclerosis

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I THINK we will all agree that perhaps the greatest challenge to medical research now is that presented by arteriosclerosis and, in particular, its most lethal manifestation, coronary artery disease. And I think we may also agree that our methods for detecting coronary disease are woefully inadequate. Completely normal findings with our most modern diagnostic techniques on one day guarantee our patient no immunity whatsoever from an attack the following day. We are, indeed, virtually blind to the presence of the disease until it suddenly strikes. The detection of advancing coronary disease in asymptomatic individuals is difficult, to say the least, but the unfortunate truth is that our methods are so insensitive we can often provide no objective evidence of its presence in patients whose typical symptoms denote advanced disease. So, we clearly need different and better methods for detecting coronary atherosclerosis and following its course. The quest for the cause of this disease and for therapeutic methods aimed at arresting or preventing its progress goes on unremittingly. If and when that ultimate therapeutic goal is reached, its effective clinical application will depend, in no small measure, on the detection of coronary atherosclerosis at an early stage in its progress, when therapy is most likely to be effective. The challenge to improve our diagnostic methods has been made and it must be met.

During the last decade the ballistocardiograph has been applied with increasing frequency to the problem of coronary artery disease. This new technique is suffering the same growing pains experienced by electrocardiography and other new methods during the early phases of their application. There is always the tendency for preliminary results to produce divergent views and con-

flicting opinions and so becloud the real issues that it is difficult for anyone outside the field to form a definite opinion; and so it is with respect to the value of ballistocardiography in the

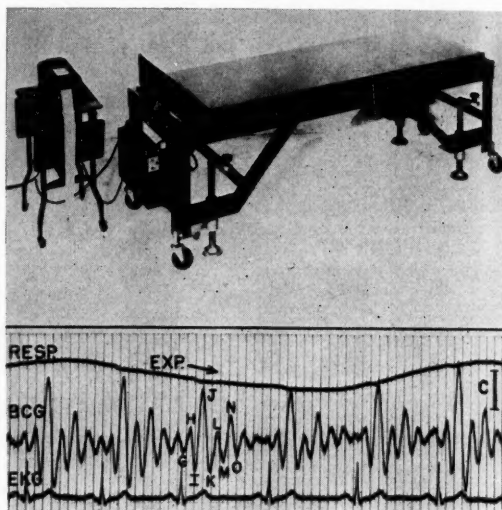


Fig. 1. (A) High-frequency ballistocardiograph, commercial model. This instrument has a natural frequency of 12 to 14 cycles per second when loaded with 150 pounds dead weight. The electronic transducer and amplifier are mounted on the foot end of the frame. (Courtesy Technitrol Engineering Co.). (B) Normal ballistocardiogram recorded with a high-frequency bed. The upper tracing (RESP) is the pneumogram (expiration downward), the middle one (BCG) is the ballistocardiogram, and the lower one is the electrocardiogram (Lead II). Heavy time lines are 0.1 second apart. The bracketed vertical line (C) in the upper right corner represents the calibration deflection (280 GM. = 1 cm.). Reproduced by permission of *American Heart Journal*.

coronary disease field. My purpose will be to examine the evidence and to try to provide you with data on which an opinion may be based.

For the benefit of those who may be unfamiliar with the method I would like to comment on it briefly.

The ballistocardiograph is an instrument designed to record the minute motions of the body

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caused by the rapid ejection of blood from the heart with each beat. The instrument shown in Figure 1 is a commercial version of the Starr high-frequency bed, which is but one of several

ballistocardiograms; even more interesting was his observation that in some of them an abnormal ballistocardiogram provided the only objective evidence of heart disease. In the years since that

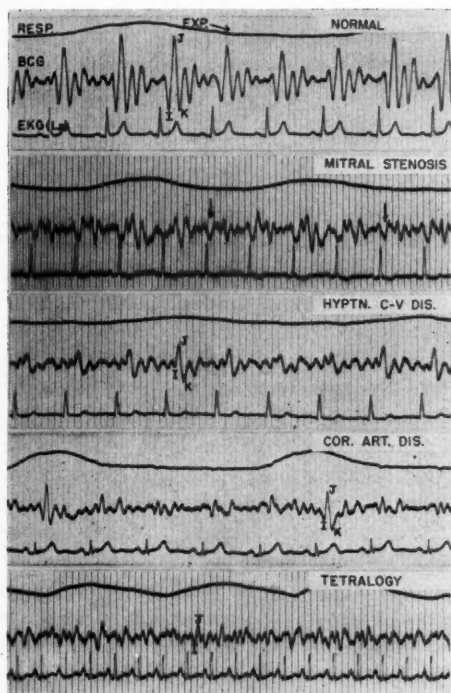


Fig. 2. The ballistocardiogram in various types of cardiovascular disease. The record at the top is a normal one for comparison.

general types in use. The ballistocardiogram is a record of the motion of the platform on which the subject reclines. The ballistocardiogram shown here is normal and is typical of those from all young healthy individuals. The pattern is consistent and repetitive. The size and form of the pattern is related to the force with which the heart ejects blood into the great vessels. However, in the heart weakened by disease this normally great propulsive force is altered and the resulting ballistocardiogram is strikingly different from the one shown here. The waves are generally smaller and the consistent pattern is usually lost.

Figure 2 shows a normal record at the top and four abnormal records from patients with various types of cardiovascular disease.

Early in his work Starr<sup>1</sup> found that many of his patients with coronary disease had abnormal

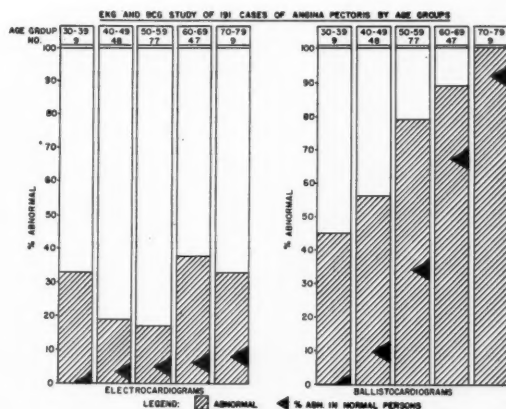


Fig. 3. Electrocardiographic and ballistocardiographic study of 191 cases of angina pectoris. There is a low incidence of electrocardiographic abnormality (24 per cent, for the whole group) and a high incidence of ballistocardiographic abnormality (75 per cent, for the whole group). The frequency of abnormal electrocardiograms and ballistocardiograms is significantly higher in the patients with angina pectoris than in the normal control subjects (arrowheads) in each decade except the eighth. There is an increasing frequency of abnormal ballistocardiograms in patients as well as in normal subjects. Only 45 per cent of the patients in the fourth decade had abnormal ballistocardiograms; this incidence rose to 100 per cent in the eighth decade. (Reproduced by permission of *American Heart Journal*)

time his observations have been repeatedly confirmed. Studies by different investigators using the Starr or the direct-body ballistocardiographic instruments on large groups of patients with either classical angina pectoris or a history of myocardial infarction have, in general, yielded similar results.<sup>2,3,4,5</sup> Since those obtained by our own group are fairly representative, we will examine them;<sup>6</sup> 328 patients were compared with 369 clinically normal subjects from twenty to eighty-four years.

On the right in Figure 3 are the results of the ballistocardiographic studies on 191 patients with angina pectoris. The height of the cross-hatched block represents the percentage of patients with abnormal records in a given decade. The ballistocardiogram was abnormal in 75 per cent of the whole group but there was a definite age trend from about 45 per cent for the thirty-year-olds to 100 per cent for the seventy-year-olds. The

black arrows indicate the results from our control group of normal persons; there were no abnormal records below the age of forty, but above this there was a steadily rising incidence of ab-

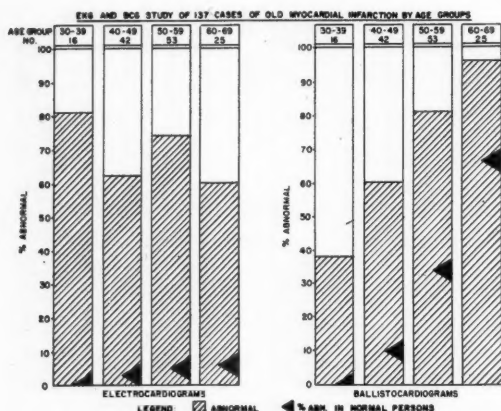


Fig. 4. Electrocardiographic and ballistocardiographic study of 137 cases of old myocardial infarction. Number of patients in each decade is indicated below the age group designation. Electrocardiograms abnormal in 69 per cent and ballistocardiograms abnormal in 72 per cent of whole group; both incidences are significantly higher than in clinically normal persons (arrowheads). There is an increasing frequency of ballistocardiographic form abnormality with age in patients with myocardial infarction as well as in normal subjects. Only 38 per cent of the patients below the age of forty had abnormal ballistocardiograms but the incidence increased to 96 per cent in the seventh decade. (Reproduced by permission of *American Heart Journal*.)

normality reaching 92 per cent of normal subjects in their seventies. The electrocardiographic results are on the left; only 24 per cent of the patients with angina pectoris had abnormal electrocardiograms.

The results in 137 patients with previous myocardial infarction (Fig. 4) are similar to those from the patients with angina pectoris. Of those below the age of fifty only about one-half had abnormal ballistocardiograms. Abnormal electrocardiograms were more frequent in this group with healed infarcts, as one would expect.

I would like to set aside for a moment the question of the causes of the abnormal records in the clinically normal subjects and assume them to be, in fact, normal and free of heart disease. From the combined results of these and other studies we may conclude: (1) that about three-fourths of all patients with coronary artery disease have abnormal ballistocardiograms, (2) that above the age of fifty abnormal records are even

more frequent in these patients, but they are also quite frequent in clinically normal persons, (3) that below the age of fifty the incidence of abnormal records is low in normals but it is also relatively low in patients with coronary artery disease. Are there any differences in pattern or waveform which would serve to distinguish between patients and normals? The answer is *no*, if we exclude the coronary artery disease patients who are in congestive failure. It would be well to point out here that there is no ballistic pattern which is typical, characteristic or pathognomonic of coronary disease. Nor do quantitative measurements of the records improve the separation of subjects with and without overt coronary disease.<sup>6</sup>

So we are forced to conclude that by itself, the resting ballistocardiogram fails to provide a satisfactory separation of the two groups of individuals. Many supplementary techniques, such as the exercise and anoxemia tests, have been used to improve the diagnostic value of both the ballistocardiogram and electrocardiogram but most of these have failed to add very much. In contrast to the results reported by Master,<sup>7</sup> our results with his "two-step" test have been discouraging.<sup>8</sup> The only "stress test" which, in our hands, has proved of definite value in separating subjects with and without coronary disease is the so-called "cigarette test." Henderson<sup>9</sup> first observed that the ballistocardiograms of patients with coronary disease frequently deteriorated after smoking a cigarette whereas this response was unusual in normal persons. Davis<sup>8</sup> of our group confirmed his results, as did Russek<sup>10</sup> more recently.

Figure 5 shows the effect of the "cigarette test" on three different subjects. In each case the record labeled A is the control, and B is the record taken immediately after smoking. The upper and middle pairs of records are from two patients with angina pectoris and both show the deterioration which marks a positive response. In the lower pair of records there is no change after smoking. This is a negative test on a normal physician.

Figure 6 shows the results of tests on the 200 subjects in Davis' original study. The cigarette test was considered positive if there were definite deterioration of the post-smoking ballistocardiogram. The height of the black bars indicates the percentage of patients with positive tests in each age group. The results from the normal subjects

are on the left, those from the coronary disease patients are on the right. The over-all average of positive tests was 7 per cent in the normals and 59 per cent in the patients, a ratio of about 8:1.

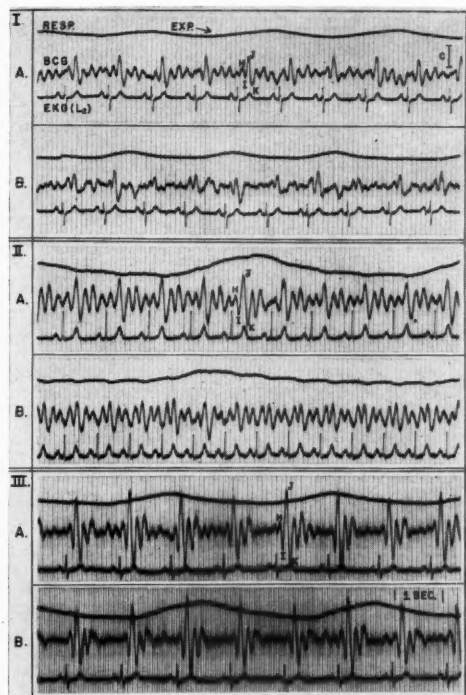


Fig. 5. The effects of cigarette smoking on the ballistocardiogram. I. A. Control record from a fifty-one-year-old man with angina pectoris; B. Ballistocardiogram immediately after smoking. Amplitude decreases, the H wave shows relative augmentation, while I and J are shortened and rounded. Blood pressure rose from 114/80 to 122/88 mm. Hg. This represents a positive test. II. A. Control ballistocardiogram from a fifty-year-old man with angina pectoris and hypertension. B. Ballistocardiogram immediately after smoking a cigarette. The G and H waves are considerably accentuated, J shortened, producing many "early-M-like" complexes. This is a positive cigarette test. Blood pressure rose from 176/106 to 204/120 mm. Hg. III. A. Control ballistocardiogram from a healthy fifty-five-year-old man, a physician. B. Record immediately after smoking. No significant change is apparent. This is a clearly negative cigarette test. (Reproduced by permission of *American Heart Journal*.)

Electrocardiographic changes after smoking were so rare that they deserve no mention. A recent summary<sup>11</sup> of our more extensive experience with the cigarette test in 450 subjects yielded results similar to these just mentioned. The use of filters or de-nicotinized cigarettes failed to protect the sensitive individuals.

The mechanism through which cigarette smoking operates to produce the ballistocardiographic changes described is not known. Nor is it clear why its selectivity is so high for patients with

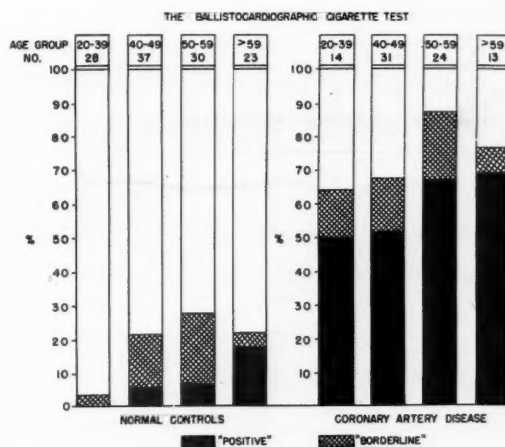


Fig. 6. The incidence of positive and borderline responses of the ballistocardiogram to smoking a cigarette in normal subjects and in patients with coronary artery disease. (The difference between normal and diseased groups is significant in each decade). (Reproduced by permission of *American Heart Journal*.)

coronary artery disease. There is evidence that nicotine is the active agent but we have as yet no proof that nicotine evokes these changes by producing coronary vasoconstriction, although we cannot deny this as a possibility. While we are not sure that the ballistic deterioration seen after smoking is caused by myocardial ischemia, we are sure that acute ischemia is capable of causing deterioration of the record. Figure 7 illustrates my point. These records are from a sixty-two-year-old man with angina who obliged us by developing a typical attack while lying on the ballistocardiograph bed. Record A was taken before the attack and is an unusually good one considering his age and his disease. Record B, taken during the attack, shows gross deterioration; no normal complexes are present. In addition, the EKG shows rather marked S-T segment depression. In record C, taken after the attack was relieved by nitroglycerin, the ballistocardiogram again resembles the control record; the EKG changes have not completely regressed. So in this case, acute ischemia produced transient abnormalities in both mechanical and electrical function.

In trying to improve the diagnostic value of the

ballistocardiograph in coronary artery disease many other leads have been followed but the results do not justify their mention here.

The one major obstacle to a complete and crit-

port this view; such evidence as does exist is indirect and circumstantial. It is certainly true that the rising incidence of ballistocardiographic abnormality with age resembles or parallels other

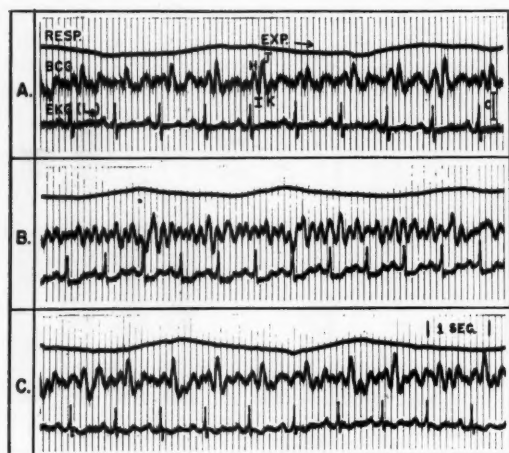


Fig. 7. The effects of myocardial ischemia on the ballistocardiogram. This series of tracings is shown because of the clear demonstration of the changes in ballistic form which occurred during a spontaneous attack of angina pectoris which developed while the ballistocardiogram was being obtained. The sequence of ballistic form changes observed in this subject is similar to that which occurs during a positive cigarette test. The subject was a sixty-two-year-old man with severe coronary insufficiency and angina pectoris. A. Control ballistocardiogram, showing some slurring of I and J, with rounding and shortening of K. B. Ballistocardiogram obtained while subject experienced pain. Gross deterioration is apparent, with short to absent I waves, distorted J and K, and relatively prominent diastolic waves. C. Ballistocardiogram nine minutes after relief of the pain by nitroglycerine. Form is in general similar to that of the control record. (Reproduced by permission of *American Heart Journal*)

ical evaluation of the ballistocardiograph as a diagnostic tool in coronary disease lies in our uncertainty as to the cause or causes of abnormal records. It has not been established that an abnormal ballistocardiogram is caused *only* by cardiac disease; nor has it been possible to estimate the relative importance of extra-cardiac factors in the genesis of these records. For this reason we cannot be certain about the significance of the abnormal records observed so frequently in older clinically normal subjects. The obvious question, whether these individuals are really free of heart disease, is one which cannot be answered. It has been suggested<sup>12</sup> that most of these abnormal records are caused by sub-clinical coronary artery disease and this seems quite possible. There is, however, no direct or conclusive evidence to sup-

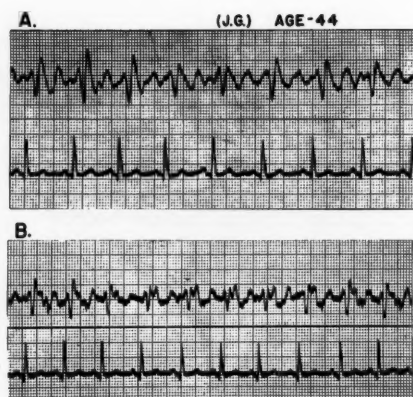


Fig. 8. The two records (high-frequency bed above, aperiodic below) from a forty-four-year-old man with coronary artery disease. The high-frequency bed record shows shortening or absence of the K wave varying with respiration. In the aperiodic bed record there appears an abnormal, headward wave (marked by arrows) in each complex, corresponding in time to the K wave in the other record, which shows similar respiratory variation. (Reproduced by permission of *Circulation*).

curves relating clinical or anatomical coronary artery disease to age.<sup>13</sup> However, this does not constitute proof that there is a direct, casual relationship between coronary disease and ballistic abnormality; the only conclusion it does allow is that both variables are related to age and may or may not be related to each other.

Here then is our impasse. On the one hand we are searching for a more sensitive method of detecting coronary artery disease, preferably one which will provide evidence of the disease early in its course, before it produces symptoms. The ballistocardiographic method gives a positive result in a very high proportion of patients with known coronary disease and also gives a positive result in about one-half of those presumably normal individuals whose ages make it likely that coronary disease is present. On the other hand, our uncertainty that the positive result is, in fact, due to coronary disease alone, demands a conservative attitude until more evidence is brought to bear.

Admitting the present inadequacies of ballisto-

cardiography, I would like to briefly discuss research efforts being made to improve the method and to clarify our understanding of the information it supplies. There is little doubt now that im-

the latter part of systole. This abnormality failed to show up in the Starr bed record.

Even at this early stage it seems certain that improvements in method will increase the specifi-

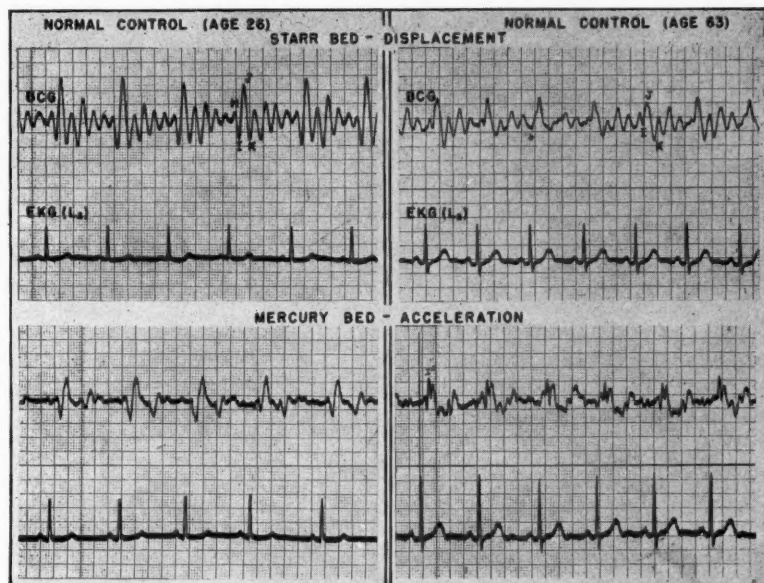


Fig. 9. Starr bed and aperiodic mercury bed records on a twenty-six-year-old normal female and a sixty-three-year-old normal male. Both records are normal in the young person, both are abnormal in the older person. In the latter, the multiple rapid forces seen in the mercury bed record are absent in the Starr bed record. (Reproduced by permission of *Bulletin of Johns Hopkins Hospital*).

perfections of the method itself are partly to blame for its limited usefulness. Serious errors are inherent in all of the standard techniques and these are caused for the most part by the body's dorsal elastic spring interposed between the body mass and its supporting surface.<sup>14</sup> Recent developments<sup>15,16,17</sup> in instrumentation now make it possible to obtain records free of this artefact, and directly related to the force applied to the body mass by cardiovascular activity; furthermore, the range of frequencies which can be observed has been extended much higher and errors in timing due to phase shift largely eliminated.

To illustrate the differences between the newer techniques<sup>18</sup> and the standard ones are the records (Fig. 8) from a forty-four-year-old man with coronary disease. Record A, from the Starr high-frequency bed, is simple in waveform and shows only slurring and shortening of the J-K segment. Record B, from our "aperiodic mercury bed,"<sup>19</sup> is quite different; it contains more rapid detail and shows an extra abnormal headward force in

city and precision of our measurements of cardiovascular force. However, there is no assurance that improved ballistocardiographic methods will permit wider separation of patients with coronary disease and older normal persons.

In Figure 9 the records on the left are from a twenty-six-year-old normal person. The Starr record is above, the mercury bed record below. Both are normal but the differences in waveform are apparent. On the right are the records from a sixty-three-year-old clinically normal subject. Both Starr and "mercury" records are quite abnormal although much of the rapid force detail in the latter failed to appear in the Starr record. Whether or not such abnormalities in the records from these older persons indicate coronary atherosclerosis is a question which remains to be answered.

Current and future research in the field of ballistocardiography must be directed toward the identification and quantitation of the numerous factors, cardiac, extra-cardiac and extra-cardio-

vascular, which contribute to or modify the basic internal force pattern. Further biophysical and physiological investigations both in man and in the experimental animal are in progress and it is hoped that these will lead to an improved understanding of cardiovascular mechanics in normal individuals as well as in patients with cardiovascular disease.

Aside from physiological research, time itself may provide some of the answers. In clinical follow-up studies on normal individuals, if those whose original records were abnormal, clearly develop coronary disease sooner or more frequently than those with normal records, then the abnormal ballistocardiogram would take on more significance.

In conclusion, I would like to summarize the views of the group which I represent regarding the clinical value of ballistocardiography in the study of patients with coronary atherosclerosis.<sup>19</sup> However promising the method may be in the future, it is at present primarily a research tool. We strongly urge that its use be confined to clinical research. The widespread application of ballistocardiography in the clinical evaluation of the individual patient could prove most dangerous for reasons which must be apparent to all.

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## Discussion

HENRY LONGSTREET TAYLOR, University of Minnesota:

The ballistocardiograph is a new device and we are still in the process of learning how to use it. The growth of knowledge regarding a procedure of this kind can at times be irregular, occasionally misleading and not infrequently discouraging. Those of us who have been working in this field have been both enthusiastic regarding the possibilities of learning something about a new aspect of the functional state of the myocardium and at the same time have been rather fearful that the technical inadequacies of the early recording instruments would lead the field into disrepute. It seems to me that Dr. Scarborough has skillfully mixed the proper amount of caution and skepticism with an adequate proportion of hope. It should be emphasized that ballistocardiography is going through a major period of instrumental development. It appears that we are on the verge of being provided with physical instruments to record the motion of the body without artifacts. Such a development will materially reduce the uncertainties that currently exist in the interpretation of ballistocardiographic records. In addition it will make it possible for the physiologist to study, with some real hope of obtaining relatively precise results, the characteristics of the internal network of arteries, tendons and other tissues which transmit cardiac forces to the mass of the body. So we should not be unduly discouraged with the obvious failure of the current ballistocardiographs to aid a great deal in the diagnosis and management of coronary disease.

Dr. Scarborough has pointed out that one of the major problems facing ballistocardiography today is the interpretation of the record which has an abnormal wave form and/or low IJ force in an otherwise healthy individual. It has been suggested by Dr. Isaac Starr and others that such individuals are suffering from what amounts to subclinical coronary artery disease. This possibility has stimulated us to examine the usefulness of the ballistocardiogram in population comparisons as well as in long term follow up studies of initially healthy individuals. Our recent comparisons of the ballistocardiographic characteristics of American and Italian men indicate some intriguing possibilities. The basic idea in this work was that the BCG age trend found in

clinically healthy American males may be different in other populations less subject to atherosclerosis and coronary heart disease. In this country samples of clinically healthy men at successively older ages from twenty to sixty show an average rise in the frequency of "abnormal" BCG records and an average decline in the I-J force. Now from such men, at some later date, the victims of coronary heart disease are recruited and we know that many of the "healthy" American males after the age of thirty-five already have marked atherosclerosis. On the other hand, men in Italy are drawn from a population in whom coronary heart disease is much less frequent than here in the United States. The fact is shown not only by vital statistics but has been verified by extensive clinical surveys and other studies by Dr. Ancel Keys and Dr. Paul D. White and their colleagues.

On some 200 Italian males in either Naples or Cagliari (Sardina) records were obtained with a high-frequency, undamped Starr Type BCG bed. These men were clinically healthy and were selected to be reasonable representative of the local population. It was found that there was no difference approaching statistical significance between the frequency of "abnormal" BCG wave patterns found in Italians and those found in Americans up to the age of sixty. It seems reasonable to conclude that the increasing pattern abnormality with age in both countries is more closely related to the aging process *per se* or to some processes associated with it, than it is to coronary artery disease. However, when we turn to the measurement of the IJ force a different picture appears. It was found that the IJ force, measured on those records in which the ballistocardiographic pattern was judged to be normal, was much larger in Italians than in Americans in the fourth, fifth and sixth decades. The possibility that these observed differences could occur by chance was less than 1 in 1000 as judged from application of the standard T test. This difference requires further investigation before one can hazard a conclusion as to its meaning. But the inference is there and it seems possible, at least, that the ballistocardiograph may develop into a useful tool in the study of the epidemiology of heart disease and that force measurements may have some prognostic significance.

All but a handful of Minnesota's eighty-seven counties will have Heart Fund chairmen for the 1956 drive in February. Field representatives from the Saint Paul office of the Minnesota Heart Association have been busy for several months recruiting local chairmen in all parts of the state. Upon accepting the invitation to serve, the typical county chairman in Minnesota becomes responsible for recruitment of city chairmen in each community within his county borders.

Working several months in advance, many county

chairmen succeed in recruiting Heart Fund solicitors at even the township level. Complete organization of the state is the ultimate recruitment goal of the Minnesota Heart Association, and volunteer workers are the lifeblood of the movement.

Since Minnesota is recognized as a world center of heart disease research, MHA feels a strong obligation to state residents to lead the way by raising many Minnesota dollars to take advantage of the wonderful research facilities existing within the state.

## Medical Emergencies in Myocardial Infarction

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**M**YOCARDIAL infarction is a consequence of locally impeded coronary flow of such degree and duration that necrosis of muscle results. Fundamentally, the sequence of events begins when two deficiencies occur: the supply of oxygen is locally insufficient to maintain equilibria vital to contemporary myocardial function, and the flow of fluid (blood) is inadequate to sweep away the end products of myocardial metabolism. Up to a point this sequence is reversible: as oxygen supply and blood flow improve, or as the load upon the heart muscle diminishes, normal function is restored. Beyond this more generalized reactions are evoked which distinguish the presence of injured, necrotic tissue.

The medical emergencies in myocardial infarction surely begin with the compelling need for accurate diagnosis, to distinguish between reversible changes in myocardial function manifest in transient abnormalities of the electrocardiogram and irreversible injury to heart muscle. Currently this rests principally upon the demonstration of changes remote from the heart itself: leukocytosis, accelerated erythrocyte sedimentation rate and fever—a series of reactions on the part of the body to the necrotic area in the heart.

To these indices of myocardial infarction there has lately been added elevated levels of glutamic-oxalacetic transaminase.<sup>1,2</sup> This enzyme is commonly present in the sera of normal adults but in concentrations less than 40 units per ml. In most patients with other signs and symptoms of myocardial infarction the serum transaminase level rises to a maximum of 100 to 300 or more units within three days after the first manifestations of pain, presumably due to release of this enzyme from damaged heart muscle, and returns to normal within a week or less. Although it requires careful preparation of reagents, and its significance as an index of myocardial necrosis is

highly questionable in the presence of liver disease, the estimation of serum transaminase level may take its place with the other tests applied to the diagnosis of myocardial infarction.

A second emergency, disorders of the heart beat, may overtake the patient without warning and sometimes with disastrous consequences. Auricular arrhythmias may further embarrass the function of the injured ventricle but are rarely fatal. Auricular fibrillation or flutter calls for rapid digitalization, if ventricular rate is rapid or signs of pulmonary congestion appear—0.8 mg. lanatocide C intravenously followed by 0.2 to 0.4 mg. in four to six hours.

Ventricular arrhythmias, on the other hand, are much more serious. At the border between the injured area and the normal ventricular muscle the products of myocardial metabolism or damage accumulate as irrigation is deficient. In this zone local excitability may become peculiarly instable. Sometimes this provokes no more than distortion of the electrocardiogram; sometimes it is manifest as a focus of ventricular extrasystoles. Neither of these phenomena is significantly dangerous to life, but when these are combined with more generalized changes in myocardial excitability or conduction, ventricular tachycardia or fibrillation may supervene. Prevention or treatment of these disorders must be based upon two factors: the influence of drugs—quinidine or procaine amide—upon excitability and conductivity in the heart muscle, and improvement of the intrinsic myocardial circulation. For ventricular tachycardia quinidine may be given in doses of 0.4 gm. every two to three hours. If arrhythmia persists this may be raised to 0.6 gm. per dose. If intravenous medication seems imperative procaine amide may be injected slowly—not more than 0.1 gm. per minute—up to a total of 1 to 5 gm. Neither quinidine nor procaine amide is indicated as a routine preventive measure. Indeed, when myocardial infarction is associated with "shock" both quinidine and procaine amide must

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Presented in the Symposium on Arteriosclerosis, University of Minnesota, Minneapolis, September 9, 1955.

## MYOCARDIAL INFARCTION—ANDRUS

be used with extreme caution since each has a tendency to provoke hypotension. Otherwise, when premature beats are observed quinidine may be employed to advantage—0.2-0.3 gm. every three to four hours.

Finally, due to the injured area of muscle, myocardial contraction and therewith ventricular stroke volume may become seriously deficient. During the acute phase of myocardial infarction a moderate and transient fall in blood pressure is not uncommon. Although this requires watching it usually passes off and is not associated with symptoms and signs of collapse. On the other hand, in about one half of the fatal instances (10 per cent or less of all cases) death is preceded by a state of "shock": severe hypotension (systolic pressure 90 mm. Hg or below) with small "thready" pulse (pulse pressure 25 mm. Hg or less) plus cold moist skin, pallor, weakness, usually tachycardia, and oliguria. The most significant factor at the basis of this complication is certainly hypodynamic contraction of the injured left ventricle with consequent reduction of cardiac output and of "effective" (intra-arterial) blood volume.\* With the critical fall in blood pressure, blood flow through the entire coronary arterial bed is diminished and to the locally damaging effects of occlusion there is added reduced irrigation of the remaining myocardium. If this circulatory state becomes established and persists recovery is uncommon.

The first step in preventing shock with myocardial infarction is to be on guard. It is by no means necessary to interrupt rest to measure blood pressure every few minutes but change in heart rate or in quality of the pulse should not fail of observation. If, as in some instances, acute hypotension is precipitated by some rapid arrhythmia this should be promptly, though cautiously, treated.

The general measures usually employed in treating myocardial infarction, particularly the use of oxygen, apply equally in the case complicated by "shock." However, one may express caution regarding morphine and a preference for meperidine (demerol—25 to 75 mg.) intramuscularly for relief of pain in the presence of hypotension.

\*In experimental animals (dogs)<sup>3</sup> there is some evidence of a mechanism, probably neurogenic, which operates when coronary vessels are occluded and which appears to inhibit a compensatory rise in peripheral resistance.

One cannot sharply distinguish fundamental differences between shock with myocardial infarction and traumatic or hemorrhagic shock, but in the first, left ventricular failure is certainly a more common complication. Digitalis should be administered if congestive failure is evident; overdosage is to be avoided.

All the methods of treating hemorrhagic or traumatic shock have been applied to the condition under consideration, including transfusion—intravenous or intra-arterial—of blood or plasma. Perhaps because the total blood volume is not commonly so critically decreased in shock with myocardial infarction—indeed, systemic venous pressure may be increased—transfusions do not seem to be so dramatically useful here as in shock following hemorrhage or trauma.

Epinephrine had been occasionally tested as a vasopressor agent in this variety of shock but only with some apprehension because of its striking action upon the rate and force of the heart beat and upon myocardial irritability. However, other drugs are now being produced in rapid succession which have the property of provoking peripheral vasoconstriction without hazardous direct effect upon the myocardium. If the treatment of myocardial infarction can be said recently to have advanced it is along the line of this adjunct.

The most potent of the available substances is 1-norepinephrine (1-arterenol) but it must be administered by vein; it causes necrosis if injected or extravasated into the muscle. Dosage: 4 to 24 cc. of 1/1000 solution added to 1000 cc. 5 per cent glucose and given by slow intravenous drip. Others suitable for intramuscular or intravenous injection have a milder and more evanescent action. These include:

N-methylphenylbutylamine sulfate ("Wyamine"): dose 35 to 70 mg. in 5 per cent glucose I.V.\*\* by slow drip or 15 to 45 mg. I.M.†

Phenylephrine hydrochloride ("Neo-synephrine"): dose 5 to 10 mg. I.M.† or I.V.\*\* (in dilute solution) every fifteen to thirty minutes.

Hydroxyamphetamine ("Paredrine"): dose 10 to 20 mg. I.M.† or 5 to 10 mg. I.V.\*\* in dilute solution.

B-hydroxy-B-(2,5-dimethoxyphenyl)-isopropylamine ("Methoxamine"): dose 30 to 50 mg. I.M.† or less I.V.\*\*

Isopropyl norepinephrine ("Isuprel") hydrochloride has proved of value in cases of shock associated with heart

\*\*I.V. = by intravenous injection.

†I.M. = by intramuscular injection.

## MYOCARDIAL INFARCTION—ANDRUS

TABLE I.<sup>7</sup> 82 PATIENTS WITH SEVERE SHOCK (CORONARY OCCLUSION) (BINDER, ET AL, 1954)

No.	Therapy	Survived	Died
22	Non-specific	4	17 (82%)
35	I.V. and I.A. Transfusion + vasopressor drugs	2	33 (94%)
25	1-arterenol	8	17 (68%)

block. Dose: 2 to 3 mg. I.V.\*\* or 7.5 to 15 mg. under tongue.

Levo-1 (m-hydroxyphenyl)-2-amino-1-propanol ("Aramine") recently introduced is described by Sarnoff, et al<sup>4</sup> as accomplishing marked rise of blood pressure from hypotensive levels, increased coronary flow and improved myocardial contraction without requiring greater coronary flow per unit of work, and without a tendency to provoke cardiac arrhythmias. These observations have been confirmed in limited clinical trial.<sup>5,6</sup> Dose: I.V.\*\* infusion - 2 to 6 cc./min. - containing 50 to 200 mg./liter.

Drs. Binder, Ryan, Marcus, Mugler, Strange and Agress<sup>7</sup> of the Department of Medicine, University of California at Los Angeles, recently tabulated the results of various forms of therapy of shock with severe myocardial infarction as reported in the literature, adding eighty-two cases of their own.

### Conclusion

In the end the outcome of any attack of myocardial infarction will be determined—barring fatal embolism—by the extent and severity of myocardial damage. By treating hypotension when it occurs one hopes to sustain the circulation to vital organs, including the remainder of

TABLE II. THERAPY OF SEVERE SHOCK (CORONARY OCCLUSION) (BINDER, ET AL<sup>7</sup> AND FROM LITERATURE)

No.	Therapy	Survived	Died
59	I.V. Transfusion	6	53 (90%)
42	I.A. Transfusion	8	34 (80%)
131	1-arterenol	53	78 (60%)

the myocardium. Combined with oxygen therapy this may limit the extent of necrosis, and improve the function of the hypodynamic left ventricle. It follows that such therapy should be instituted as early as possible after the blood pressure falls. It is seldom necessary to raise the systemic pressure above 120 mm. Hg. If it is elevated too fast or too high, pulmonary edema may be precipitated. If signs of pulmonary congestion accompany shock, one must resort to rapid digitalization. Judging from one's own experience and from the results reported by others, it may be possible to rescue perhaps twenty per cent of otherwise fatal cases of myocardial infarction by therapy with vasopressor drugs.

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Dollars donated by Minnesotans make up the Heart Fund. The drive has been conducted since 1949, when the Minnesota Heart Association was founded by a group of physicians. Since 1951, the February drive has been conducted by the Minnesota Association of Life Underwriters.

Heart Fund dollars go to support a three-point program of research, education and service. Major emphasis is placed on research support. But the Heart Fund dollar also is used to bring helpful information to the heart patient, and to help keep Minnesota physicians abreast of new developments in diagnosis and care of cardiac patients.

The greatest foe of the heart research scientist is time, the relentless ticking of the clock being a constant

reminder to him that while he struggles to unlock the secrets of Nature, human beings are dying of the disease he battles.

The conquest of heart disease is only a matter of time, the scientist knows. But will the answers come today, tomorrow, or a decade from now?

Today, a little girl whizzes down the sidewalk on her tricycle because research found a way of closing a hole in her heart. Today, a businessman is back at his desk because research discovered drugs that can lower his elevated blood pressure.

These answers came in time for some . . . too late for others. Research supported by funds from the Minnesota public is the answer to this question of time.

# Evaluation of Status and Results of Management in Coronary Heart Disease

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**M**ORE than one hundred and fifty years ago Jenner<sup>1</sup> expressed the fear that the medical world may seek in vain for a remedy for coronary atherosclerosis. Today with brighter hopes but still with a meager background of fundamental knowledge, we are witnessing thrusts into the unknown which may provide sound discoveries in the treatment and prevention of atheromatosis. Until such effective measures become available, the physician can only strive to alleviate some of the consequences of this baffling disease by applying the lessons learned from his daily encounter with civilized man's greatest killer.

Throughout the history of medicine the use of a multiplicity of drugs and procedures in treating a specific illness has usually been the earmark of therapeutic failure. The prevailing tendency appears to be to overtreat patients with coronary disease than otherwise. It should be recognized that under proper supervision a large proportion of these cases will run their course from beginning to end with little or no medicine, and this often with significant advantage. Nevertheless, the advent of new methods for the prevention and treatment of complications arising in the course of coronary atherosclerosis has led in many quarters to the adoption of "routine treatment" for all cases. While many components of such routine programs are extremely valuable, they lose their value when indiscriminately and at times unnecessarily employed. In recognizing that judicious use of various drugs may relieve suffering and save lives, sight must not be lost of the fact that the major part in the control of this disease still lies in expert guidance in making the mental and physical adjustments which will enable these patients to carry on within their capacity without symptoms.

Presented in the Symposium on Arteriosclerosis, University of Minnesota, Minneapolis, September 9, 1955.

## Angina Pectoris

In the general management of patients with angina pectoris or other forms of myocardial ischemia, a more realistic approach has been taken in recent years to insure that restrictions imposed are carefully individualized not only on the basis of coronary reserve but also in terms of the total life situation in each case. It seems reasonable to advise patients with angina to hold a normal weight. Although there are some conflicting data regarding the relationship between obesity and life expectancy,<sup>2-4</sup> the clinical observation that reducing the obese cardiac helps to decrease the work of the heart cannot be challenged. The apparent correlation between fat and cholesterol in the diet and atherosclerosis has led Keys<sup>5</sup> to advocate the avoidance of obesity and "periodic gorging," restriction of extractable fats to not over 25 to 30 per cent of total calories and perhaps restriction of cholesterol to under 1 gram a week.

*Alcohol.*—Alcohol has long been known to be a depressant of the central nervous system capable of decreasing anxiety and promoting a sense of well-being. It has a beneficial psychic effect upon some patients with angina pectoris and is often of value in relaxing tension at the end of a working day. In spite of strong evidence to the contrary, alcohol is still widely regarded as a potent coronary vasodilator, second only to the nitrites. The failure of alcohol to influence the electrocardiographic response to standard exercise in coronary patients<sup>6</sup> indicates, however, that its ability to relieve anginal pain is based solely on a sedative action (Fig. 1). Since the administration of ethyl alcohol prophylactically may not only create a false sense of physical fitness but remove the protection afforded by angina, the danger of its employment prior to contemplated exertion should be recognized. The calorie content of alcohol also cannot be disregarded (100 proof liquor contains 100 calories to the ounce),

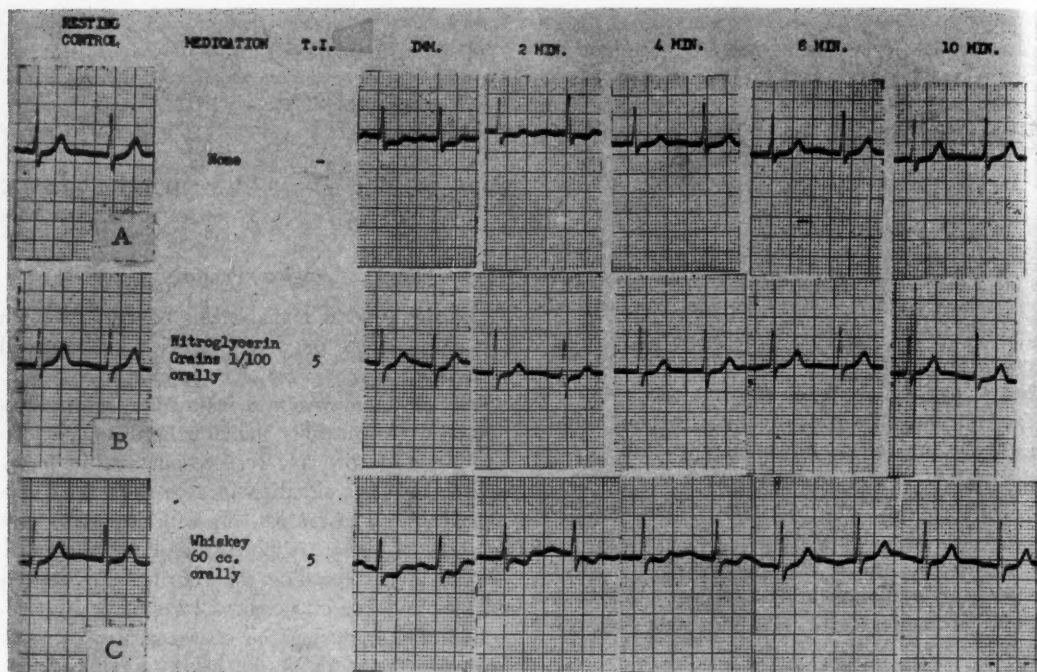


Fig. 1. Electrocardiograms (lead CF) showing modifying influence on resting control of standard exercise. (Master two-step test). Response A follows no medication; response B follows 1/100 grain (0.4 mg.) glyceryl trinitrate sublingually, time interval (T.I.) five minutes. Response C follows 60 cc. whiskey orally, time interval five minutes.

nor can its tendency to stimulate the appetite. One may therefore conclude that alcoholic liquor should not be a routine prescription for all patients and should no longer be regarded as possessing coronary vasodilator properties.

**Tobacco.**—Although there is no convincing proof that tobacco directly causes or intensifies the average case of angina pectoris, it has become common practice for physicians to advise against its use in all patients suffering from this affliction. As Sprague<sup>7</sup> has stated, "A doctor who cannot contemplate life without tobacco is hardly objective about the dangers of smoking." Because of the enjoyment afforded and the emotional satisfaction obtained some believe that patients with inactive forms of heart disease should be permitted to smoke in moderation.<sup>8,9</sup> Although there are no valid experimental data on the effect of nicotine on the coronary arteries or on the heart, numerous investigations have clearly shown an augmentation of the systolic and diastolic blood pressures, heart rate and basal metabolic rate in response to smoking. Tobacco

also exerts well-known vasoconstrictive effects on the peripheral circulation even in normal subjects. These observations have led to the belief that smoking may exert an adverse influence on coronary circulation. Davis and associates<sup>10</sup> suggest that changes in the ballistocardiogram produced by smoking may be the result of nicotine action on the hypothalamic-posterior pituitary axis, with resultant release of vasopressin (Pitressin), which acts as a coronary vasoconstrictor. Our own studies<sup>11,12</sup> in patients with coronary disease have failed to confirm this mode of action of nicotine. Thus glyceryl trinitrate in almost all instances did not modify or prevent ballistocardiographic changes induced by smoking, and Pitressin, even in large dosage, failed to mimic the nicotine effect on ballistic pattern. Paradoxically, whiskey was found to block the ballistic changes in some patients who exhibited marked sensitivity to nicotine. In the light of previous evidence based on electrocardiographic tests<sup>6</sup> this could not be accepted as evidence of a coronary vasodilator action induced by alcohol. These observations were therefore interpreted as

# CORONARY HEART DISEASE—RUSSEK

indicating that the ballistic response to smoking is evoked primarily by peripheral vascular constriction and not by alterations in coronary blood flow. Consequently it would appear that smoking

the modifying effect of varying amounts of nitroglycerin (1/300 to 1/50 grain) upon the electrocardiographic response to standard exercise has shown that individualization of dosage is an im-

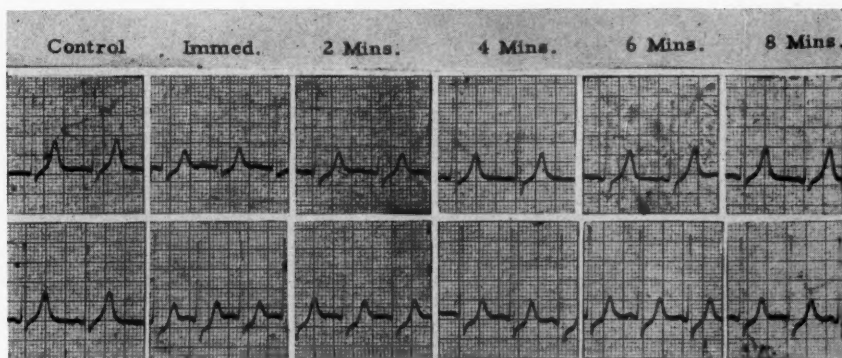


Fig. 2. Upper row, Master two-step test (lead  $V_4$ ) in a patient with coronary disease. Lower row, the same test has been repeated following grain 1/150 nitroglycerine. Note more abnormal response following nitroglycerine.

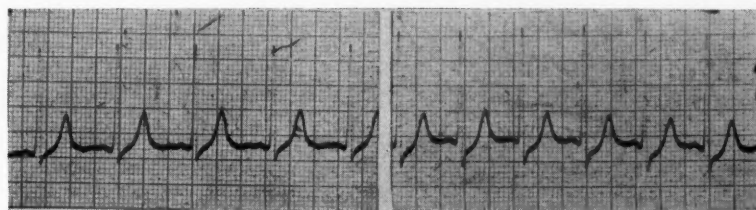


Fig. 3. (Lead  $V_4$ ) in same patient as in Figure 2. At left, patient is resting supine. Tracing at right was recorded five minutes after 1/150 grain of nitroglycerine.

does not present a direct danger to the patient with coronary disease through coronary vasoconstriction and that whiskey is not an effective coronary vasodilator and antidote for nicotine with respect to the heart. The antagonism between these drugs is exhibited almost entirely on the peripheral circulation. With respect to the heart, each increases the tendency to tachycardia and ectopic beats. The known cardiovascular, local and systemic effects of smoking clearly establish the inadvisability of the continuance of this habit in patients with heart disease.

**Medication.**—Nitroglycerin still remains the most useful drug in the management of angina pectoris. Although great difficulty often exists in convincing the patient to use it as freely as necessary, it has not been adequately appreciated that the drug also possesses latent potentialities for adverse effects in this disease. A study of

important prerequisite to rational therapy in angina pectoris.<sup>13</sup> In exercise tests 10 per cent of patients responded paradoxically to the drug as a result of venous pooling in the lower extremities, diminished venous return to the heart and reduced coronary blood flow in spite of concomitant coronary vasodilatation. These undesirable effects were prevented by reduction in the dosage of nitroglycerin and lessened by the application of elastic bandages to the lower extremities. The optimum dosage for most patients was found to be 1/300 to 1/200 grain sublingually. The precipitation of acute myocardial infarction appears to be more than a theoretic danger from overdosage during treatment of the anginal attack (Figs. 2 and 3).

Because of the relatively short duration of the action of nitroglycerin, the search has continued for a long-acting coronary vasodilator which is capable of reducing the frequency and severity

# CORONARY HEART DISEASE—RUSSEK

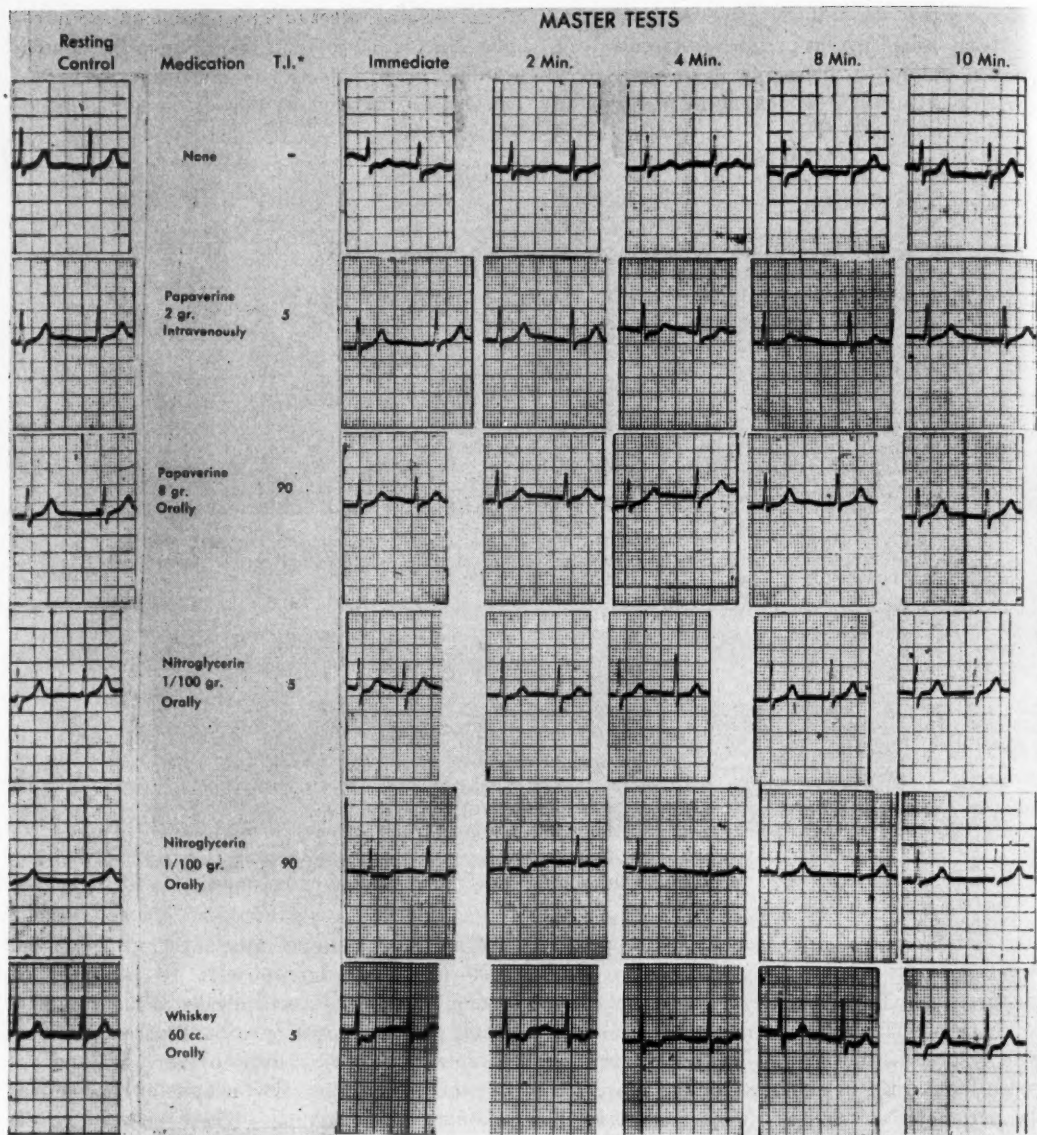


Fig. 4. Master test responses (lead V<sub>4</sub>) in a patient with coronary insufficiency with and without the administration of drugs.

\*T.I., time interval (minutes) between medication and beginning of test.

of anginal attacks by routine daily administration. Many drugs have been characterized by their individual sponsors as fulfilling this need but few have been able to withstand the test of time and clinical usage. Realizing the difficulties in clinical evaluation which is dependent solely on the relief of pain, we have attempted, during the past six years, to employ an objective method based on the electrocardiographic response to the

Master two-step test in carefully selected patients.<sup>14-17</sup> Our conclusions may be summarized as follows:

Papaverine, in spite of the disappointing results reported by others, appears to be an effective coronary vasodilator when prescribed in a dosage two to four times greater than that in common usage (Fig. 4). Dioxylone (paveril) phosphate, when administered in doses similar to those em-

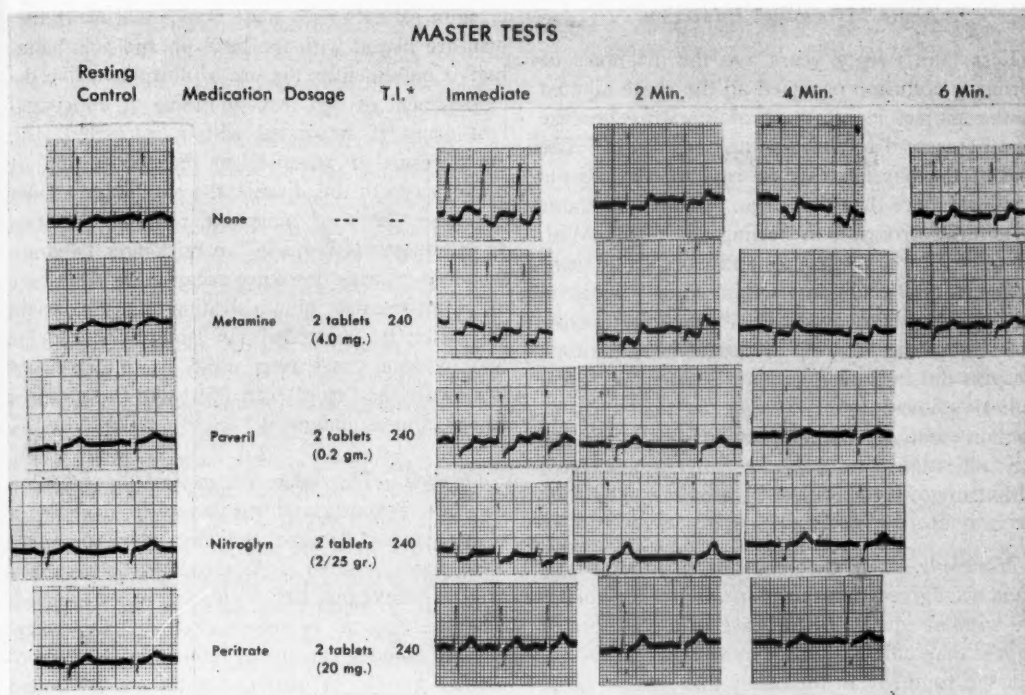


Fig. 5. Master test responses (lead V<sub>e</sub>) obtained in a patient with angina pectoris with and without the administration of drugs.

\*T.I., time interval (minutes) between medication and beginning of test.

ployed with papaverine did not give comparable results. Paveril appeared to be a much less potent drug than papaverine according to this method of testing.

**Xanthine Drugs:** Aminophylline in the dose of 7½ grains intravenously or 6 grains orally was found to have slight to insignificant effect. Choline theophyllinate, which has recently been acclaimed by some groups,<sup>18</sup> appeared to be ineffective in the recommended dosage of 200 mg. four times daily. When this dose was quadrupled, however, benefit was noted in some patients but gastric distress was common.

Khellin even in massive dosage failed to alter favorably the electrocardiographic response in all patients tested.

Octyl nitrite by inhalation was at best as effective as 1/300 grain nitroglycerin.

**Heparin:** Much interest has been shown recently in the influence of heparin on various cardiovascular phenomena including lipid transfer in blood, reduction of the significant Gofman ultracentrifuge flotation fractions, and anginal

pain. Our own observations<sup>19</sup> as well as those of others<sup>20,21</sup> have failed to confirm any influence on anginal pain or on exercise tolerance determined electrocardiographically.

Roniacol, tetraethyl ammonium chloride and Priscoline were without demonstrable value.

Metamine (triethanolamine trinitrate biphosphate) was found to exert little or no significant effect on the electrocardiographic response to standard exercise.

Nitroglyn (glyceryl trinitrate in sustained-action tablets) gave disappointing results in spite of logic behind its use. Dosage as high as 4/25 grain was without effect in a large proportion of patients.

Peritrate in 10 to 20 mg. dosage afforded protection for four to five hours after an initial lag of 1 to 1½ hours before its action became apparent. Of all the drugs tested, Peritrate appeared to be the most effective long-acting coronary vasodilator for the clinical management of angina pectoris (Fig. 5).

### Acute Myocardial Infarction

Less than twenty years ago the diagnosis of coronary occlusion occupied all the space allotted to the subject in our medical literature because therapy seemed to be so limited and futile. The role of the physician in the care of his patients was little more than that of an attentive spectator of nature's processes of healing and repair. With the advent of new concepts and methods of management this traditional regimen of "watchful waiting" has been gradually replaced by a positive therapeutic program of "active intervention." Despite the improved prognosis attending these radical innovations in therapy, no unanimity of opinion exists, even among authorities, regarding the indications, results and dangers associated with many of the specific measures now employed.

*Morphine.*—For the relief of pain all physicians are agreed that morphine and other opiates are without equal. In the past an initial dose of no less than half a grain of morphine was recommended routinely in the belief that smaller doses do no good and that substitutes are worthless. In spite of its wide use, little is known of the effects of morphine on the coronary arteries although the vague notion exists that the drug exerts a direct beneficial action in coronary thrombosis independent of its influence on symptoms. Experimentally, morphine given intravenously has been shown to produce increased coronary flow of brief duration in animals with acute myocardial infarction<sup>22</sup> but clinical confirmation of this action has not thus far been obtained. Although its characteristic influence on pain was clearly apparent, no significant effect on the electrocardiographic response to standard exercise (Master two-step test) has been observed from the use of the drug in patients with angina pectoris.<sup>18</sup> On the other hand, morphine sometimes complicates the course of coronary thrombosis. Its undesirable actions in producing abdominal distension, urinary retention, respiratory depression, vomiting and retching are well known. Morphine causes strong vagal stimulation, rendering the heart more susceptible to ventricular ectopic rhythms; it increases biliary pressure and exerts an antidiuretic and hypotensive effect. In doses of about 15 mg. the drug has no effect on the circulation in recumbent patients but may precipitate a hypotensive syncopal attack or col-

lapse in patients with acute myocardial infarction who are placed with the head up and feet hanging. Consequently, the use of morphine, like the employment of bed rest, quinidine or anticoagulant drugs is associated with a calculated risk. As a result of advances in the recognition of milder cases of this disease, the old dictum calling for large doses of morphine routinely as soon as the diagnosis is made can no longer be countenanced. Large doses are occasionally necessary as is intravenous administration, but mild pain can often be controlled by demerol or codeine and in some cases even these are unnecessary. Obviously, no "rules" can ever take the place of sound clinical judgment.

*Oxygen.*—The value of oxygen in relieving dyspnea, cyanosis and cardiac pain in cases in which cardiac damage and circulatory derangement have resulted in a secondary generalized arterial anoxemia has been clearly established. The question as to whether or not hyperoxygenated blood is capable of influencing local myocardial anoxia in patients with uncomplicated myocardial infarction, however, has not thus far been satisfactorily answered. In normal animals which admittedly have no functional collaterals, administration of oxygen has proved valueless in experimental occlusion.<sup>23</sup> In other studies<sup>24</sup> on anesthetized dogs, however, it has been shown, using platinum electrodes, that there is a statistically significant increase in available oxygen in border zones surrounding areas of infarction after pure oxygen breathing. Fifty per cent oxygen proved greatly inferior to pure oxygen in achieving favorable results. These observations support the belief that inhalation of high concentrations of oxygen may reduce the extent of muscle necrosis resulting from coronary occlusion in man.

On the other hand, in the anesthetized animal, one does not encounter the psychogenic influences evoked by the administration of oxygen in the human subject afflicted with coronary thrombosis. Administration of oxygen to most patients carries the implication that they are critically ill. The claustrophobia which some patients develop on being placed in an oxygen tent is well documented. Administration of oxygen by nasal catheter frequently leads to irritation or inflammation of the pharynx which cause hacking and coughing, both undesirable efforts. The use of

a mask often produces paradoxically a sense of suffocation and a state of anxiety. Such factors surely contribute to the total work of the heart and, therefore, are likely to nullify or even overbalance any advantages to be gained from the relatively little additional oxygen which can be added to the blood in patients with uncomplicated myocardial infarction. With the concentrations of oxygen attainable in the use of a tent only 1.6 cc. of the gas can be added to each 100 cc. of blood. Nearly twice this amount can be added if the patient inhales 100 per cent oxygen.<sup>25</sup> The effect of this therapy on the electrocardiographic response to standard exercise using the Master two-step test has been studied in a series of patients with angina pectoris.<sup>26</sup> It was found that the administration of 100 per cent oxygen did not prevent the RS-T segment and T wave changes induced by exercise and failed to hasten the disappearance of these manifestations of myocardial anoxia. The administration of 100 per cent oxygen, moreover, failed to prevent the onset of anginal pain or to influence its duration. Indeed, some observations in which exercise response actually deteriorated under oxygen therapy suggest that hyperoxygenated blood may interfere with compensatory coronary vasodilatation evoked by local myocardial anoxia.

It is concluded, therefore, that oxygen should be freely employed in acute myocardial infarction when an indication for its use is recognized or even suspected. Its continuation, however, should be based on evidence of objective or subjective improvement of the symptom for which it was administered. It would appear that the indiscriminate use of oxygen may contribute nothing to the patient's ultimate recovery and yet add considerably to his anxiety and discomfort during the most acute phase of the disease. In the uncomplicated case even the high concentrations obtainable with a mask have questionable value, but if oxygen is to be used at all only this method of administration would seem to deserve consideration.

**Anticoagulants.**—Although anticoagulant therapy has become an accepted form of treatment of acute myocardial infarction, there is still much disagreement, even among authorities, regarding the indications for its use. The statistical data presented by the committee on anticoagulants of

TABLE I. MORTALITY RATE AND INCIDENCE OF THROMBO-EMBOLIC COMPLICATIONS

	No. of Cases	Mortality		Embolization	
		No.	%	No.	%
Total	1047	350	33.4	63	6.0
Good risk	489	15	3.1	4	0.8
Poor risk	558	335	60.0	59	10.6

the American Heart Association, as well as that recorded from numerous other sources, indicate that anticoagulant drugs exert a markedly favorable influence on both the death rate and the thromboembolic complication rate in unselected groups. In spite of this convincing evidence, none of these studies have actually shown that clinically mild or low risk groups share in the overall benefit derived from this form of therapy. There is, in fact, a growing weight of opinion in favor of withholding these agents from patients who have had a clinically mild infarction.

It has been shown that the mortality rate and incidence of thromboembolism are so low among patients sustaining an "uncomplicated" first attack<sup>27</sup> that anticoagulant therapy with its attendant dangers from hemorrhage could scarcely be expected to influence the prognosis favorably in this low risk group (Table I). The objection raised against flexibility of therapy relative to our judgment of the severity and anatomy of the attack, is that one cannot always be sure of what constitutes a small myocardial infarct and further that what starts as a mild attack may become severe a few hours later. In a recent study in which anticoagulants were intentionally withheld in 122 patients with acute myocardial infarction because of the absence of certain poor prognostic signs\* at the time of the first examination, we have found that the preventable mortality under ideal anticoagulant therapy could not have exceeded 0.8 per cent.<sup>28</sup> In the entire series not a single instance of cerebral or peripheral arterial embolism was encountered. Clinical thromboembolic phenomena occurred in four patients, an incidence of 3.3 per cent. In two of these four

\*Patients were considered to be "good risks" when none of the following poor prognostic signs were observed on the day of admission to the hospital: (1) previous myocardial infarction, (2) intractable pain, (3) extreme degree or persistence of shock, (4) significant enlargement of the heart, (5) gallop rhythm, (6) congestive heart failure, (7) auricular fibrillation or flutter, ventricular tachycardia, or intraventricular block, and (8) diabetic acidosis or other states predisposing to thrombosis.

patients moreover, the diagnosis of this complication was only presumptive. The risk of thromboembolism in such cases therefore may be equalled or exceeded by the dangers attending the use of anticoagulants. After careful consideration of all clinical and autopsy data Wright<sup>29</sup> recently estimated that 1.7 deaths per 100 cases were the result of anticoagulant therapy itself.

It is difficult to translate the carefully controlled experiments of the committee on anticoagulants, under ideal conditions in research hospitals, to the every day treatment of coronary disease in practice. The imperfections, failures, and inherent dangers in this form of therapy even in the hands of the most competent investigators however should leave little hope of improving the prognosis in "good risk" cases with the anticoagulants now available and the current method of control. In this group, the small risk of thromboembolism without such treatment does not appear to justify the use of a procedure that itself may lead, even if infrequently, to serious complications and death. The occurrence of poor prognostic signs in a "good risk" patient at any time in the course of his convalescence certainly should establish the need for intensive anticoagulant therapy, but, in our experience such a development after the first forty-eight hours following the attack is relatively infrequent. It is therefore concluded that anticoagulant therapy for "mild" attacks is a costly, burdensome, and unnecessary form of treatment. Ample evidence exists to justify "prognostic classification" as a means of selecting patients for anticoagulant therapy in acute myocardial infarction.

It has been repeatedly claimed that old age provides a special indication for the use of anticoagulant drugs in acute coronary occlusion. We have shown that no justification exists for the concept that age is an important factor in determining the prognosis in the individual patient.<sup>30</sup> Statistically, there is a higher incidence of serious attacks among older patients and consequently a more frequent occurrence of thromboembolism. For this reason alone, anticoagulants have shown a greater life-saving action in patients over the age of sixty than in those below this age. Our comparison of cases of similar severity in different age groups have demonstrated repeatedly that the chances for surviving an attack of myocardial infarction are correlated not with age but with

the severity of the clinical picture. One must therefore conclude that the initial clinical appearance of the patient, irrespective of age, constitutes the best index to his future course and is the deciding factor regarding the need for anticoagulant therapy.

Out of a total of 1,318 consecutive admissions for acute myocardial infarction, 611 (46 per cent) qualified as "good risk." When account is taken of the patients with mild attacks who are treated at home by conservative measures and the persons with serious episodes who manifest contraindications to anticoagulant therapy probably no more than 30 per cent of all patients can be considered candidates for this form of treatment. This low figure however should not detract from the value of anticoagulant therapy in properly selected patients (those with poor prognostic signs), since its administration in such instances constitutes a major advance in the treatment of this disease.

*Hospitalization.*—The wide employment of anticoagulant drugs in acute coronary thrombosis has been associated with a risk commonly overlooked. In order to institute treatment without delay many patients are rushed to the hospital shortly after the onset of their clinical attack despite the fact that the highest death rate in this disease prevails during the first forty-eight hours. Since these early deaths are the result of ventricular fibrillation, cardiac asystole, shock or congestive heart failure and are unrelated to thromboembolism, they almost certainly cannot be prevented by anticoagulant drugs. The desire to save the small proportion who may die from thromboembolism after the first week may therefore jeopardize the chances for survival of the much larger segment of coronary cases known to die from other causes during the first two days. For many patients, being jostled in an ambulance or admitting office, then subjected to the psychic trauma of a hospital room and bed and of being placed in an oxygen tent, often when oxygen is entirely unnecessary, and being repeatedly punctured for prothrombin and coagulation times, hardly constitutes optimum management during this early critical period. In most instances, any form of treatment deemed necessary can be initiated in the patient's own home and removal to hospital can be accomplished if indicated, when this critical period has passed.

*Bed Rest.*—One of the major problems in the management of patients with myocardial infarction involves the decision concerning the duration and rigidity of restriction of activity. A little more than a decade ago even the milder cases were nursed in bed for at least eight weeks and were "guarded by day and night nursing and helped in every way to avoid voluntary movement or effort." The tendency to reduce the bedfast time of patients with myocardial infarction appears to be a forward step. Since cardiac work tends to be less in the sitting than in the recumbent position the "chair" treatment advocated by Levine cannot be challenged on the grounds of failing to give maximum rest to the heart. This method obviates some of the well known harmful effects of strict bed rest, permits easier commode privileges and protects against the great bedpan hazard.

The wisdom of utilizing chair treatment during the first few days of the illness, however, should be questioned. Considerably more than one half of all the deaths in this disease occur during the first two days and, even in the mildest cases, a high proportion develop suddenly within the first forty-eight hours. Many of these early fatalities are the result of cardiac standstill, ventricular fibrillation, shock or congestive heart failure. For this reason it would seem best that the patient be disturbed as little as possible during the first few days of his illness. The hypotensive effect of the opiates when the head is elevated and the feet are dependent must also be considered when "chair" treatment is to be employed soon after the onset of the attack. Most physicians appear to share the view that chair treatment offers little advantage over bed rest when such measures as deep breathing, freedom of movement, and mild exercise of feet and legs are permitted. Dependency of the legs with the patient seated in a chair would appear to predispose to thrombotic complications rather than to prevent them. Nevertheless, in the presence of dyspnea and pulmonary congestion the venous pooling produced by lowering of the legs should not be minimized as a therapeutic measure. Some physicians advocate the use of the bedside commode while paradoxically cautioning against the risk of chair treatment. The tendency of patients nursed in this manner to take too light a view of their illness and to disregard protective restrictions has been emphasized by various authors.

#### *Transfusions, Vasopressor Drugs and Digitalis.*

—If further improvement in the prognosis of acute myocardial infarction is to be obtained, the problems involved in the prevention and treatment of the severer grades of shock and congestive heart failure must be solved. It has been claimed that protracted shock, if survived predisposes to a greater or less degree of congestive failure at an early date. Evidence has been presented which suggests that the prompt and efficient treatment of cardiogenic shock may well be the means of preventing the subsequent development of congestive heart failure.<sup>31</sup> The latter may, therefore, be anticipated on occasions and necessary measures taken in advance. The treatment of severe shock following acute myocardial infarction is a challenging and usually frustrating experience because of the mortality rate in excess of 80 per cent of cases, the confusion of procedures advised and the futility of most management. The value of the usual non-specific measures, of transfusions and of various vasopressors has been difficult to assess because of a lack of uniformity in criteria for the classification of shock. There is little evidence that intravenous transfusion alone is of value in the treatment of severe coronary shock. In some instances patients so treated fare worse than do comparable patients who are treated non-specifically. Intra-arterial transfusion is not associated with a higher incidence of relief of shock or of survival when compared to a valid control series. To date, the most encouraging results have been reported with vasopressor drugs, notably levarterenol, which may reduce the mortality some 20 per cent.<sup>32</sup> Because the mechanism of coronary shock remains obscure, present day therapy continues to be largely empirical. The relative importance in the pathogenesis of coronary shock of decreased cardiac output, cardiopulmonary reflexes and peripheral vascular collapse remain to be assessed.

In summary it would appear that the maintenance of a safe, yet comprehensive therapeutic philosophy in the treatment of the patient with coronary disease demands utmost circumspection to insure that both the science and the art of medicine are being utilized wisely.

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## Discussion

HOWARD B. BURCHELL, Mayo Clinic: Dr. Russek has adequately outlined the current thoughts, accepted advances, and controversies in the management of persons with coronary disease, and there is no need to rediscuss all the specific details of treatment. I would beg the indulgence of the symposium members in re-emphasizing the background, or frame of reference, into which the detailed therapeutic manipulations which Dr. Russek has described must be placed.

We still have the serious problem exemplified by the individual who may have been assured by a competent cardiologist that he had a normal heart, and yet that day even die suddenly or have an acute myocardial infarction. We may recognize that a patient, for instance an executive who might be referred to one of us for study, must have some pathologic quanta of coronary disease, but at the present time we have no way of

accurately predicting its extent or its possible future manifestations. Thus the management of the adult population in general with *silent* coronary disease greatly overlaps the management of patients with *manifest* coronary disease. The importance of coronary disease as a cause of death has been repeatedly emphasized, and when we studied the medical deaths due to heart disease in our own city of Rochester in the years 1952-1953, we found that in 55 per cent coronary disease was the important factor, valvular and other disease affecting the heart trailing far behind. Of these individuals who died of coronary heart disease, 34 per cent died with an acute myocardial infarction.

We must suspect coronary disease in many in our adult population even when they do not give a history of, or a clue to, its presence.

As further evidence for this assertion, Dr. Achor in

## CORONARY HEART DISEASE—RUSSEK

our Clinic, studying the records of patients who showed a healed infarct of the heart at post mortem examination, found that in somewhat over a third a presumably accurate history did not contain the information suggesting the infarction nor had the diagnosis been made. He found also, in agreement with the reports of others, that in nearly 10 per cent of all people dying and having a post mortem examination a healed gross infarct will be found.

In the past few years our approach to an attempted understanding of the clinical problem presented by coronary disease has been analysis of how individuals die with an acute infarction, and how they die if they have recovered from an acute infarction.

TABLE I. ACUTE MYOCARDIAL INFARCTION AT NECROPSY IN 133 CASES (1946-1950 Inclusive)

Apparent main feature in death	Per Cent
Heart failure (including shock).....	52
Sudden death (arrhythmia?).....	24
Rupture of heart.....	15
Thrombo-embolism.....	6
Systemic 3%	
Pulmonary 3%	
Miscellaneous.....	3

In Table I are the results of the work carried out with Dr. McQuay and Dr. Edwards in respect to the deaths occurring from acute infarction of the heart to indicate the therapeutic problems. One may see that there is a large number of individuals who have a persistent "coronary insufficiency" state, or a "coronary failure" manifested by angina following their acute infarction, but pathologically no further actual infarction or secondary coronary thrombosis has been found. A large number of the patients in this category die suddenly within a week or so of their major infarction. It is seen that heart failure is responsible for nearly 50 per cent of deaths if all types are combined; presenting predominantly as right heart failure in nearly one-fourth of the cases and as left heart failure, as recurrent pulmonary edema, in considerably less than that. Approximately 10 per cent died from shock which was initiated by, and persisted after, the acute infarction, and in this study 15 per cent died of rupture of the heart. Only 6 per cent died of thromboembolic disease. Implicit in this table are the therapeutic goals for the attempted control of the morbidity and mortality of acute myocardial infarction, namely the understanding and prevention of sudden death, of heart failure, shock, rupture, and thromboembolism. I believe that definite progress has been made in each of these problems, as discussed by Dr. Russek, but advance has been indeed limited.

Regarding anti-coagulant therapy, it is my practice to give anti-coagulants routinely to everyone admitted to the hospital in whom the diagnosis of an acute myocardial infarction is made. Most patients in the Rochester area are admitted to the hospital when this diagnosis is made. We are willing to give anti-coagulant therapy to 100 or more patients with the hope of preventing one death. (That is, if 20 patients were to die out of the 100, and 5 per cent of these were to die related to

thromboembolism, then one, that is, 5 per cent of the 20, might be saved by anticoagulants).

I had the opportunity of looking over Dr. Russek's paper, and as a spring board for a discussion of differences, I refer to the sentence, "The risk of thromboembolism in such (low risk) cases may be equaled or exceeded by the dangers attending the use of anticoagulants." I believe that it is just in such low risk cases that the dangers of anticoagulants are minimal, its control most readily achieved, and the salvage possibilities of the patient most complete. Some evidence has been presented indicating that anticoagulants may increase the incidence of myocardial rupture, but this has not been established in our own experience. It may be pointed out that if anticoagulants do decrease the number of deaths in patients with acute myocardial infarction and if the number of ruptured hearts remained the same in the absolute scale, then the relative percentage of ruptures, as observed by the pathologist, should show a slight increase.

I believe that there is some danger from pericardial hemorrhage when a complicating pericarditis is present, but this is minimal.

I found that I was in no disagreement with Dr. Russek's discussion of what has been called the chair treatment of myocardial infarction. It is my belief that the perspective concerning this particular therapy has become distorted. The program of getting the patient out of bed for a short period of time each day involves perhaps only 5 to 10 per cent of the twenty-four-hour period. I think that the same goal may be achieved by allowing activity and postural change in a proper cardiac bed. Incidentally, I do not believe that it is particularly paradoxical to allow the patient to use the bedside commode and not go through the routine of getting him into a chair for short periods of time each day. As I have visited various hospitals and talked to patients who have been treated for acute myocardial infarction outside our own city, I do not see a great deal of difference in the way the majority of patients are treated. There are occasional ones, however, where to my mind an unnecessary period of strict bedrest has been enforced, and to have the individual flat in bed or to be fed by an attendant seems not only completely unnecessary but probably detrimental to his physical and psychic recovery.

TABLE II. CAUSE OF DEATH IN 250 CASES OF HEALED MYOCARDIAL INFARCTION

Etiology primarily cardiac origin	Cases	Per Cent
Congestive heart failure without acute myocardial infarction.....	44	17.6
Acute cardiac death ("sudden death") without congestive failure or acute infarction.....	64	25.6
Deaths during episode of recurrent acute myocardial infarction.....	49	19.6
Total.....	157	62.8

If the individual survives an acute myocardial infarction, what is the future course? Dr. Achor has studied the hearts of individuals who have shown the scar of a healed myocardial infarction, and Table II

(Continued on Page 917)

# ***Surgical Treatment of Arteriosclerosis***

## **The Challenge of Arteriosclerosis to Surgeons**

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**T**HE challenge of arteriosclerosis, as revealed in any well considered analysis of the problem, cannot be surgical but must be medical. Certainly it is true if we accept this premise: the kind and the quantity of fat taken up from the diet by the body largely determines the intensity of the arteriosclerotic process. Therefore, a medical regimen that prophylactically manages the lipid uptake problem has the most to recommend it. Just as a vaccine is demonstrably superior to an antibiotic, so does medical prevention assume a greater role than mere surgical correction of existing and continuing disease. Although both disciplines will have important contributions to make in succeeding years, our hopes for future generations must inevitably abide largely with the former. The medical man, with an assist from the biochemist, must assume and cannot shirk from the prime obligation to establish an effective management for this problem. The magnitude of this issue, in terms of lives lost or burdened by crippling handicaps, is of the foremost order. Here, therefore, is *the* challenge: control this condition of such widespread influence that it more frequently than any other process shortens and damages the lives of adult Americans.

From poignant personal experiences I am quite aware of appetite's damaging betrayals. I am therefore convinced that an effective medical regimen must overcome the handicap of these recurring individual dietary indiscretions. Many and sympathetic discussions with those who are also overweight have established that viewpoint. Certainly, too, this objective of limiting one's fat consumption must be brought about without any very stringent regimentation of the dietary habits, —if it is to be adopted widely by all who need this

help. Knowing about the disadvantages of an excessive caloric intake is no assurance that the person will forego such indulgences. Those in the ranks of the internists are no thinner than the individuals from any other specialty, at least not until we examine those hapless ones frightened by a train of symptoms which stems from a site of vascular insufficiency. That this widespread habit of overeating is more deep seated psychologically than some easily maneuvered emotional quirk is also denied by the robust contour of our psychiatric associates. To summarize, there is a thin fraction spartan-minded about their diet or so naturally endowed with the gaunt habitus as to carry some protection from the degenerative effects of an excess fat intake. For the bulky remainder, until there becomes available a medical means of guarding our health in spite of one's overeating, the surgical challenges created by the arteriosclerotic remain.

The problems of arteriosclerosis exist close at hand in any general surgical practice. The frequency of arteriosclerosis is increasing; and the total number of cases is on the upgrade as well, from an enlarging percentage of our population that have lengthier lifetimes in which to acquire this affliction.

Surgeons' accomplishments in response to the arteriosclerosis challenge have, through the years, scarcely been brilliant or imaginative. They have long viewed the toes withering from vascular insufficiency only to respond by separating this unfortunate man from his leg. The relatively recent use of sympathectomy as a prophylactic measure, probably was the initial substantial benefit resulting from their thinking in terms of an extremity saving concept.

For those persons suffering from vascular insufficiency, better means are now available for providing relief—and without loss of limb. Under appropriate circumstances after an endarter-

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ectomy, or a grafting procedure which removes or shunts around a diseased area, considerable or even complete relief from the previously inadequate blood flow can be realized. However, one should not sing of this very loudly for it is but a modest triumph. Although temporary benefits can be brought to a large number of these people, the malady lingers on.

There is a considerable need for more accurate, more sensitive, means of detecting and evaluating this disease's extent. Our rate of progress in mastering this clinical problem seems sure to hinge upon finding a solution to that need.

Required too is superior vascular prosthetic equipment. Whether of artificial or natural origin, it seems reasonable to require that these devices should possess a durability, in years of good function, at least equivalent to the vascular endowment of man at birth. Degeneration, thrombogenicity, disruption, deterioration, and aneurysm formation involving and adjacent to the replacement currently crop up to limit the percentage of successes below the ideal. In connection with these above-cited problems peculiar to vascular anastomoses is the pressing need for an efficient, and preferably quick, method for uniting small vessels (2 mm. and under), and then, to be sure, have the result invariably function. Existing suture techniques in this area leave much to be desired and failure by thrombosis promptly or in the early postoperative period is disturbingly frequent. This deficiency in our knowledge looms as an especial disadvantage in contemplated dealings with direct anastomoses of systemic vessels to coronary arteries of limited initial diameter, further attenuated by arteriosclerosis.

Too, it is an inescapable conclusion that for some time to come vital organs will continue to be discovered as diseased only after they have been virtually destroyed by advanced stages of arteriosclerosis. Their replacement will be required if life is to be saved. The immunological problems of such homologous transplants appear far from insoluble even from this contemporary view of our medical future. And when we can predictably introduce homologous organs, having them survive functionally, surgery will indeed have come of age medically. Into the foreground of that bright vista projects again the critical need for reliable techniques of coupling small vessels.

The surgeon faces an arresting challenge and

has an intriguing opportunity to devise means of controlling the total lipid uptake from the intestinal tract. It would appear that nature has designed an alimentary system which has proven to be unnecessarily efficient. Perhaps from an anthropological point of view we have not acquired an adequate compensatory hypertrophy of those neural centers regulating appetite. Such a neurophysiological approach to this problem should prove both exciting in its potential and rewarding in its results. In any event, since the bulk of our population now consumes excess amounts of fat beyond the actual quantity needed or even desirable for most of these individuals, catabolizing this overabundant, and ultimately hazardous, intake is impossible and hence incompletely done. From the continuing transport of, and contact with, these damaging residues arise the arteriosclerotic vascular difficulties.

Essentially the problem is to devise means that will overbalance the normal lipid metabolism in favor of the intestinal residue. The net barrier between gut and lymph or blood vessels must be upped a bit. Several possible means arise for countering this eventually disastrous state. One approach might be a reduction in the area available for intestinal absorption, as after an intestinal bypass procedure. Yet another plan might seek control of enzymatic or other chemical aids to fat absorption through a reduction in the external secretion of the pancreas or by external sequestration of bile salts from the intestine. The unique enterohepatic recircularization of the latter offers intriguing possibilities. Finally, we might modify lipid absorption through techniques designed to reduce the amount of fat reaching the blood via the major lymph channels. A limited accomplishment by any of these designs could slow down the crippling or fatal progress of arteriosclerosis. Actually, with the evidence already at hand from certain clinical observations, one is permitted the perhaps ingenuous prediction that if through one or a combination of these procedures, the dietary lipid uptake were stringently reduced, a definite, albeit limited, degree of reversal in existing arteriosclerotic processes would take place.

When one reflects for but a moment on the great loss in life induced by arteriosclerosis, it is anomalous that, proportionally, so little experimental work on this problem is currently under way in surgical laboratories.

# Occlusive Arterial Disease

## *Management by Thromboendarterectomy*

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CLINICAL investigations of the past five years have shown that the peripheral ischemic manifestations of arteriosclerosis may often be due to localized lesions in one of the major arteries. Willis has recently reviewed the evidence that the well-known localization of the early intimal lesions of arteriosclerosis to certain susceptible portions of the major arteries may be explained on an essentially mechanical basis.<sup>1</sup> It appears also that hemodynamic factors associated with the flow and coagulation of blood cause the subsequent arterial obstruction to become localized to only a segment of the arterial tree.<sup>2</sup>

Numerous reports of surgical experiences have indicated that restoration of blood flow through a segmentally occluded artery may now be successfully accomplished. Surgical efforts have been directed along two essentially parallel lines: (1) resection of the diseased arterial segment and replacement by arterial, venous, or synthetic grafts; and (2) resection of only the inner layers of the occluded arterial segment and reconstitution of a new artery using the preserved and relatively undiseased outer layers of the original artery.<sup>3-21</sup>

The relative merits of the two methods—resection with graft versus thromboendarterectomy, as the latter procedure is called—have not as yet been fully determined. Although the purpose of this paper is to present our experiences with thromboendarterectomy, it will be readily apparent that most of the factors contributing to the success or failure of this method also apply to any of the various techniques of resection with grafting. The primary limitations to either approach appear to be those imposed by the nature of the disease.

Between January, 1951, and July, 1955, at the University of California School of Medicine and

the Veterans Administration Hospital in San Francisco, thromboendarterectomy was performed ninety-nine times in ninety-seven patients for the treatment of segmental arterial obstructions due to arteriosclerosis.\* At the beginning of this period, thromboendarterectomy was a new operation and hence in an exploratory phase. Since that time, numerous modifications have been made, not only in the operative technique but also in devising more accurate diagnostic methods, in the selection of patients, and in postoperative care. A steady improvement in morbidity and mortality figures has resulted. It is believed that, owing to these improvements, a majority of the complications which occurred early in our series could now be avoided.

Full and accurate definition of the extent of arterial disease is of prime importance in the proper selection of suitable candidates for operation. In all cases, operation was performed for lesions involving a segment of the arterial tree between the upper abdominal aorta and the popliteal bifurcation. Thromboendarterectomy distal to the level of the popliteal artery has not proved to be technically feasible. Translumbar aortography, which affords roentgenographic demonstration of this entire area, has become the most useful method for arteriographic visualization. Details of the technique of aortography currently employed have been described in another publication.<sup>22</sup>

In patients shown by arteriography to have diffuse arterial disease and/or multiple segmental occlusions, the operative complications were increased and the circulatory improvement was less satisfactory. In selected cases, thromboendarterectomy of a high level segmental occlusion may be warranted even in the presence of a lower in-

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\*Ten patients in this series are being reported through the courtesy of Louis G. Brizzolara, M.D., Chief of the Surgical Service, Veterans Administration Hospital, San Francisco, California. Dr. Brizzolara has used a technique of operation identical to that reported in this paper.

# THROMBOENDARTERECTOMY—WYLIE

operable occlusion if, by this means, partial revascularization of a severely ischemic extremity can be accomplished.

Arteriograms may disclose stenosis of a major vessel, rather than complete obstruction. A stenotic lesion of arteriosclerosis, when it exists as the sole impediment to blood flow, is particularly amenable to endarterectomy, and inasmuch as such lesions are believed to be precursors of complete occlusion, they are a strong indication for operation.<sup>22</sup>

In general: in our experience, the higher the level of occlusion, the more localized has been the disease and the more satisfactory the results from operation. The most favorable lesions have been those that involve the aorta and common iliac arteries. A combined lesion which obstructs the external iliac artery on one or both sides as well not only presents a greater surgical problem but also frequently indicates the presence of diffuse arteriosclerosis with spotty changes in the more distal vessels. The lower lesions causing occlusion of the superficial femoral artery have been least favorable for thromboendarterectomy. The experiences from this study have shown that femoral thromboses, though usually segmental, are commonly associated with lesions at other levels. Accordingly, the long-term value of operations at this level is lessened. Furthermore, the incidence of both immediate and late post-operative thromboses has been greater with operations at the level of the femoral artery than with operations at higher levels. Accurate pre-operative assessment is based upon arteriographic demonstration of all the occluding and stenotic lesions and can rarely be made by physical examination alone.

One particular clinical finding has become important, however, in the selection of patients for operation. It has been disappointing to find that the more severe forms of peripheral ischemia were rarely associated with single segmental arterial obstruction. Patients with rest pain or gangrene were found in most cases to have multiple occlusions or other evidence of diffuse disease, and thromboendarterectomy was therefore seldom feasible. An exception has been the patient with a sudden solitary occlusion. In such a situation, sufficient collateral circulation has had no opportunity to develop, and advanced lesions and often gangrene may be precipitated. In the absence of other contraindications, arteriograms

TABLE I. THROMBOENDARTERECTOMY—SEGMENTAL LOCALIZATION. 99 OPERATIONS, 97 PATIENTS

Site of Obstructive Lesion	Thrombosis	Stenosis	Total
Aorta	2	2	4
Aorta and bilateral common iliac	29	11	40
Bilateral common iliac		6	6
Unilateral common iliac	15	7	22
Aorta, bilateral common iliac, unilateral external iliac	3	1	4
Unilateral common and external iliac	3		3
External iliac	3		3
External iliac and common femoral	2		2
Common femoral	2		2
Superficial femoral	12	1	13
Total	71	28	99

have been performed in all patients with severe ischemia in order to find the infrequent patient who may be benefited by operation.

The technique of thromboendarterectomy currently employed has been described in detail in another publication.<sup>23</sup> The following résumé is a brief description of the method. Preliminary exploration determines the extent of gross intimal disease, particularly with reference to the lower level of sclerosis. After mobilization of the diseased segment, systemic heparinization to last one to two hours is induced. Clamps are then placed to isolate the occluded artery. The artery is opened by a continuous longitudinal incision. A subintimal cleavage plane is reached by a circumferential incision into the intima below the lower level of gross intimal thickening and beveled upwards to leave a smooth lower surface. By proximal dissection, the obstructing intima with the enclosed thrombus is peeled away from the outer media to a point above the proximal level of occlusion and is then excised. The residual media is then closed by a continuous suture and the clamps are released. In rare instances of suspected weakness of the media, fascia lata sleeve reinforcement is used. No anticoagulant drugs are given during or after operation, other than the single injection of heparin which is effective only during the period the obstructing clamps are in position and during a portion of the first hour of restored blood flow.

Table I indicates the level of the occluded or stenotic arterial segments upon which thromboendarterectomy was performed. Such a listing does not, however, describe the full extent of the operation. In most of the cases classified as unilateral iliac artery involvement, thickened intima was removed from all or a portion of the opposite iliac artery and the terminal aorta as well. Further, it was usually necessary to excise thickened

# THROMBOENDARTERECTOMY—WYLIE

TABLE II. CLINICAL STATUS FOLLOWING THROMBOENDARTERECTOMY

	Aorto-iliac	Ilio-femoral	Total
Circulation restored	50	12	62
Circulation improved	16	4	20
Circulation unchanged	1	4	5
Circulation decreased	0	0	1
Amputation	0	5	5
Death	4	2	6
	72	27	99

intima where it extended distally into the proximal portion of the external iliac artery in order not to leave a projecting ledge distal to the endarterectomized zone. In cases of aortic thrombosis, the proximal level of obstruction ranged from a point just above the aortic bifurcation to as high as the level of the renal arteries. The preponderance of aorto-iliac operations in this series reflects the greater tendency for high level lesions to be segmentally localized rather than the natural incidence of all peripheral arteriosclerotic lesions. Early in the study, it became apparent that the failure rate for operations at the femoral artery level was prohibitively high. Accordingly, the latter half of the series is composed almost entirely of operations for lesions proximal to the femoral artery.

Table II indicates the clinical results from thromboendarterectomy in terms of evidence of circulatory improvement. Amplification is necessary to make the grouping meaningful.

By "circulation restored" is meant that there was clinical evidence of return of normal circulation, that a minimum of one pedal pulse was palpable in each extremity upon which operation had been performed, and that all symptoms of ischemia were relieved. (Anatomical variations are such that occasionally only one pedal pulse is normally palpable.) Successful cases in which an attempt was made to restore normal blood flow to only one extremity in a patient with bilateral disease are included in this category. Patients whose main channel was open but in whom one or more branches, i.e., the inferior mesenteric or hypogastric arteries, remained occluded, are included in this category.

By "circulation improved" is meant that there was evidence of improvement but not full restoration of peripheral blood flow. When a sympathectomy was performed at the time of thromboendarterectomy, the improvement must have been greater than would be expected from sympathectomy alone.

Included in this group also are patients who were essentially asymptomatic postoperatively, but in whom neither pedal pulse was palpable. Fifteen of the patients in the improved group had occluded arterial segments distal to the operated segment prior to operation. There were three patients who developed distal thrombosis at the time of operation but who had improved peripheral circulation postoperatively even in the presence of this complication. In one patient with acute occlusion and a devitalized extremity, a locally successful thromboendarterectomy increased blood flow to the degree that amputation was successfully performed at a lower level than would normally have been considered necessary. For this reason, the patient was judged as improved. There were two patients with aorta and bilateral iliac operations who developed postoperative thrombosis of one common iliac artery with no improvement in the corresponding extremity. However since in both of these patients, patency of the aorta and the opposite common iliac artery caused restoration of normal flow to the other extremity, they are also included in the improved category.

"Circulation unimproved" implies that the signs and symptoms of peripheral ischemia were unchanged after operation. All five patients in this group developed local thrombosis at the operative area within an hour of operation.

Patients who are listed under "amputation" are those in whom the gangrene which necessitated subsequent amputation was a direct result of an unsuccessful thromboendarterectomy, or in whom there was no improvement in the level of amputation for pre-existing gangrene even though patency of the operated segment was maintained. Disruption of the suture line requiring arterial ligation in two patients and local thrombosis in two others were the factors precipitating gangrene in four of the patients in this group. In one, spreading infection from a gangrenous toe necessitated amputation.

For the purpose of operative evaluation only, we have included under the heading "deaths" those patients who were believed to have died as a direct result of operation. There were two deaths from hemorrhage—one at thirty-six days after operation from disruption of the aorta, and the other on the first postoperative day due to intraabdominal bleeding from an undiscovered source. Two patients died from renal failure on

# THROMBOENDARTERECTOMY—WYLIE

the seventh and ninth days respectively. One died from an unconfirmed coronary occlusion on the second postoperative day and one from pulmonary congestion on the third day. Five of the six patients who had died had regained normal peripheral circulation prior to death but are not so classified. Fatal cerebral vascular accidents developed in two elderly patients late in their postoperative courses (on the ninth and twentieth days respectively), but in view of their otherwise

TABLE III. ARTERIAL STATUS FOLLOWING THROMBOENDARTERECTOMY

	Aorto-iliac	Ilio-femoral	Total
Operated segment patent:			
—pedal arterial pulses palpable	54	15	69
Operated segment patent:			
—distal artery occlusion preoperatively	11	4	15
—distal artery thrombosis resulting from operation	3	1	4
Operated segment thrombosed:	4	7	11
	72	27	99

TABLE IV. OPERATIVE COMPLICATIONS

Complication	Postoperative Clinical Status					
	Circulation Improved	Circulation Unchanged	Circulation Decreased	Amputation	Death	Total
Local thrombosis:						
Aorto-iliac	2	1			1	4
Ilio-femoral		4		2	1	7
Local aneurysm formation:						
Aorto-iliac	1					1
Ilio-femoral						
Arterial disruption:						
Aorto-iliac					1	1
Ilio-femoral				2		2
Distal arterial thrombosis:						
Aorto-iliac	2					2
Ilio-femoral	1		1			2

normal circulatory status, these patients are not listed in the operative death category.

The cases in which thromboendarterectomy was performed have been separated into two categories on the basis of anatomical position of the arterial segment. Patients listed in the "aorto-iliac" group were those in whom operation was confined to the aorta and common iliac arteries, whether or not distal lesions were present. Patients undergoing operations upon the external iliac or femoral arteries, and those who had aorto-iliac operations which included the external iliac or femoral vessels are listed in the "ilio-femoral" category.

In the aorto-iliac group, sixty-six patients (92 per cent) developed restored or improved peripheral circulation after thromboendarterectomy, compared to sixteen (59 per cent) in the ilio-femoral group. Operation was followed by decreased circulation or amputation in one (1.4 per cent) of the former group, and in five (18 per cent) of the latter.

Table III indicates the status of the major arteries following operation. Of the patients who had the aorto-iliac operation, local postoperative thrombosis occurred in four (5.5 per cent). In the ilio-femoral group, this complication occurred in seven (25 per cent). The higher incidence of local thrombosis in operations involving the

external iliac or femoral arteries may be attributed to two factors. The arterial segments denuded of intima in operations upon the femoral or external iliac arteries are of greater length than in higher operations and the arterial caliber is decreased and usually more irregular, all of which are factors predisposing to thrombosis. Further, with the lower obstruction, it is usually technically difficult to create a smooth lumen at the lower end of the dissection owing to the extensive intimal thickening beyond the obstructed segment.

Apprehension on theoretical grounds has deterred many surgeons from using thromboendarterectomy as a method of restoring blood flow through thrombosed arterial segments. The potential complications from removing through long incisions all but the media of a major artery have caused many to direct their efforts toward the use of arterial or synthetic grafts as an alternative. The anticipated complications have been local thrombosis, local aneurysm formation, disruption of suture lines and distal thrombosis due to ischemia from the prolonged application of occluding clamps. The incidence and significance of these complications encountered in our series are tabulated in Table IV.

Local thrombosis in the operated segment occurred in eleven patients. (In all cases, throm-

basis developed in the first hour after operation.) There are three possible mechanisms which may account for the production of local thrombosis. Animal experiments have shown that a thin layer of clotted blood lines the endarterectomized arterial wall as soon as blood flow is restored and eventually organizes to become the new intima.<sup>24</sup> The rapid flow of blood in the center of the artery is believed to be the factor restricting clotting to the slow-moving outer lamina of the moving column of blood. The small arterial caliber and the luminal irregularity that are encountered after femoral and most cases of external iliac thromboendarterectomy would tend to enhance the outer clot formation and are believed to be factors in the higher incidence of local thrombosis in the ilio-femoral group as compared to the aorto-iliac group. Unnecessary manipulation of a freshly operated artery, by disturbing the layered clot, could also contribute to thrombosis.

The experiences in this series have indicated that two other mechanisms of local arterial occlusion are probably more significant than this strictly local process. Slowing of blood through the new segment by occlusion or irregularity of the distal lumen has frequently been encountered. The commonest cause of thrombosis, however, appears to be that which arises from clot formation in the static column of blood immediately distal to the lower clamp during the time this clamp is in place. Unless prevented or mechanically removed, such a clot will act as a dam to blood flow and cause blood to clot in the proximal operated segment. It is now the practice to assure patency of the distal segment before the artery is closed by observing whether retrograde flow occurs upon release of the distal clamp. If such flow does not begin, the distal vessel is manually milked proximally to clear it of inlying clot. Clotted blood or intimal fragments may also accumulate above the proximal occluding clamp, causing later embolic occlusion at the first major bifurcation in the endarterectomized arterial segment. To clear the proximal segment, the upper clamp is now temporarily opened for a few seconds before final closure of the arteriotomy incision. The risk of thrombosis after thromboendarterectomy from one of these latter mechanisms is shared by those using the resection-graft technique and may explain the not uncommon early local thrombosis described in some of the

homograft reports. Systemic heparinization during the time arterial clamps are in position tends to decrease this risk. The absence of postoperative thrombosis at any time other than during the first hour after operation indicates that anticoagulants are of no real value after this period.

Aneurysmal dilatation of the endarterectomized segment has apparently occurred in one patient in our series. The patient's local physician reported by letter that this complication developed asymptotically two years after thromboendarterectomy for thrombosis of the abdominal aorta. In this case, reinforcing fascia lata was used at the time of operation. However, the patient has not been available for aortographic confirmation of this complication. It has not been the practice in our clinic to obtain routine aortograms for follow-up study, and it is possible that undiscovered arterial dilatation has occurred in other patients.

Arterial disruption adjacent to the suture line occurred in two patients in the ilio-femoral group and in one patient in the aorto-iliac category. In the latter patient, disruption of one iliac artery on the twenty-fifth postoperative day was successfully repaired by suture and local reinforcement with a fascia lata sleeve. However, this patient died on the thirty-sixth day from disruption of the aorta. The two patients with femoral disruption were those in whom the arterial wall was so friable at re-operation that ligation was necessary to control the bleeding, resulting in gangrene and amputation. Disruption occurred on the tenth and fifteenth days respectively. Early concern over this complication led us to advocate the use of reinforcing fascia lata sleeves whenever undue weakness of the media was suspected. This method was used in only fifteen patients, however, and it may be less important than originally believed.

Distal arterial thrombosis during the time of operation was surprisingly rare. A factor in the reduction of this hazard may be the increase in collateral arterial flow which occurs in the presence of chronic occlusion. Temporary systemic heparinization should further minimize this complication.

The development of thrombosis in or distal to the operative area as a result of operation is not so disastrous to the clinical status as had originally been supposed. There were fifteen patients who developed either local or distal arterial throm-

bosis. Two of this group died of unrelated causes. Of the remaining thirteen, peripheral circulation was improved in five, unchanged in five, and decreased in three. The decrease was to such a degree in two patients that amputation was required.

The predominant symptom for which thromboendarterectomy was performed was claudication. In all patients listed in Table II as "recovered," this symptom was completely relieved; in the "improved" group, it was lessened. Reference has already been made to the relative infrequency of operable segmental lesions in patients with manifestations of more advanced circulatory impairment. There were only eighteen patients with rest pain, gangrene, or ulceration. In thirteen of this group, arteriograms revealed extensive occlusive disease. In eleven, the operated segment was in the external iliac or femoral arteries; in two, there was distal inoperable occlusive disease in association with an operable aorto-iliac thrombosed segment. Sixteen of the eighteen patients with rest pain, gangrene, or ulceration were relieved of their ischemic manifestations following thromboendarterectomy. Two have subsequently died from cerebrovascular thrombosis, and two have had amputation performed for recurrent thrombosis in the affected extremity one year after thromboendarterectomy.

Important in the total assessment of any therapeutic procedure is the long-term evaluation. The longest follow-up period in our series now approaches five years. Of the eighty-two patients in the "recovered" and "improved" groups, seventy-five have been available for personal follow-up examination. Sixty-five are alive with no change in circulatory status of the operated extremity. The average postoperative period in this group is three years. Arterial thrombosis at or adjacent to the site of operation occurred in five patients (four were in the ilio-femoral group)—three at one year, one at three years, and one at four years after operation. Cerebrovascular thrombosis occurred in four patients—on the ninth postoperative day in one, on the twentieth day in one, two years postoperatively in one, and four years postoperatively in the fourth. The first two patients died as a result. Thrombosis occurred in arteries to another extremity in three patients. Occlusion of the coronary artery developed over two years after operation in five patients, three of whom died from

this complication. One patient died from carcinoma of the kidney. A possible aneurysm has appeared in one.

The early postoperative circulatory result has been sustained in a higher percentage of patients who had aorto-iliac operation than in those who had the ilio-femoral operation. Of the original twenty-seven patients in the latter group, sixteen were improved postoperatively but only six were alive three years after operation without circulatory evidence of advancing disease in the operated extremity.

### Summary

Thromboendarterectomy has been used ninety-nine times in ninety-seven patients in the treatment of segmental arterial occlusion. Seventy-two patients had obstructions in the aorta and common iliac arteries; twenty-seven had obstructions in the ilio-femoral vessels. Sixty-two patients were completely relieved of all ischemic manifestations of arterial obstruction, and twenty were significantly improved. The factors contributing to the success and failure of this operation are analyzed on the basis of selection of patients and operative technique.

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# THROMBOENDARTERECTOMY—WYLIE

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## Discussion

DR. C. WALTON LILLEHEI: Arteriosclerosis is mankind's greatest killer at the present time. This has been emphasized repeatedly during this three-day symposium. Reference to the vital statistics for any recent year will emphasize this fact even more graphically. For example, in 1953 in the United States the number of deaths attributable to arteriosclerosis totaled more than twice those due to cancer, all accidents, and all infectious diseases combined. Despite the magnitude of this problem of arteriosclerosis and despite its complexities as to etiology as have been emphasized by many of the preceding speakers, there is a simple aspect to the problem also. Arteriosclerosis kills by mechanically occluding the blood flow to three or four vital areas of the body. These areas are: the brain, the heart, kidneys, and the lower extremities. Historically, surgery has always been at its best in dealing with mechanical obstructions. There are no more brilliant chapters in the history of medicine than the results of surgical relief of mechanical obstructions in the urinary tract, the biliary tract, and the intestinal tract. Thus, there exists in these mechanical obstructions in the blood vessels due to atherosclerosis a tremendous potential field for future development of surgical forms of management. I have said in the past and would like to repeat here again today my belief that if one were able to put the energies of all of the surgeons of the world to work exclusively on this problem at the present time, there would still be more work to be done than could be accomplished.

It was some of these thoughts that have occupied our attention during the past four years' time that we have utilized endarterectomy in this hospital. We have been particularly interested in: (1) the technical factors contributing to success or more pertinently to failure, (2) the long term results in patients with successful endarterectomies, (3) the application of these techniques to other organs such as the heart and the brain.

In regard to technical considerations that lead to success the following listed have been the most important

in our experience: (1) At the time of surgery retrograde blood flow from the distal end of the opened artery is essential. (2) Some method of sewing down the distal intima seems necessary in many cases. Most successful in our experience has been cutting the vessel off completely and making a direct anastomosis end-to-end of the endarterectomized segment to the distal un-endarterectomized but patent artery. (3) Where applicable, multiple incisions to remove the diseased intima rather than laying the entire length of the artery open are useful. (4) Sewing up the artery over a temporary splint such as a piece of appropriately sized plastic tubing is helpful in obtaining an even calibre in the endarterectomized segment. (5) Heparinizing the patient during the actual period of arterial occlusion but not in the postoperative convalescent period.

A few slides\* will illustrate the clinical application of several of these principles. The first series of photographs illustrate an endarterectomy in progress from the iliac artery on the right side down to the popliteal artery. We are entirely in agreement with Dr. Wylie in his statement that by and large endarterectomies in this segment of the arterial tree over such a long length of occluded artery have been less successful. However, this particular man has done well and his postoperative arteriogram two months later is shown in this slide. He has been followed for two and one-half years now and has shown no evidence of recurrence of his obstruction, adding additional evidence to our belief that successful endarterectomies do stand up well over time.

\*Slide presented cannot be reproduced here.

The next series of slides are from a man who had an aortico-iliac endarterectomy. His postoperative aortogram is shown here for comparison with the preoperative picture. He too has had no evidence of recurrent obstruction in the two years since surgical removal of the thrombotic occlusion of this terminal aorta.

The next slides show the opened left common iliac artery of a patient who died eight months after a successful endarterectomy. This man returned to the hos-

pital seven months after his endarterectomy because of a cerebral-vascular accident. He died one month later from this condition. At autopsy the opportunity was thus presented for studying this endarterectomized segment, and it was possible to see the very smooth lining that had developed to reline this endarterectomized segment. This lining undoubtedly comes from the blood cellular elements as well as endothelial cells of the capillaries in the remaining arterial wall which is of course viable.

As previously mentioned, we have been particularly interested in the possible application of these techniques to the coronary arteries. In this regard and illustrated in Figure 1 is a very favorable circumstance which has been established by past studies of coronary artery pathology. These studies have indicated that 75 per cent of the fatal or serious coronary occlusions occur in the first 5 centimeters of the left or right coronary arteries, and paradoxically the distal coronary arterial tree in many of these same patients is but little involved or even normal in its appearance. Dr. Karel Absolon, of our surgical staff, with the co-operation of Dr. James Dawson, department of pathology, has studied a number of the hearts in older patients and has routinely carried out coronary artery endarterectomies in the autopsy room in these fresh specimens to ascertain the feasibility of this procedure as well as to develop suitable surgical techniques. Here is a photograph of the coronary endarterectomy specimen from a sixty-year-old man. I would emphasize that these are not the coronary arteries themselves, but are the diseased and obstructing lining removed from this man's right and left main coronary arteries. Here is another similar specimen from a fifty-five-year-old man.

One has but to look at these specimens to know that were these obstructing sequestra removed successfully during life that these patients could not possibly have had other than an augmented coronary flow. Dr. Absolon has accumulated an immense amount of valuable information in these studies, and perhaps the most valuable point of all has been the realization from this work that the coronary arteries are large enough to work upon successfully by direct methods.

With these facts established Dr. Absolon and Dr. Aust, of our resident staff, have in the experimental laboratory regularly been anastomosing *in vivo* the coronary arteries of dogs. Here is a photograph taken at operation of a direct end-to-end anastomosis in a dog between the internal mammary and the circumflex branch of the left coronary artery. These operations are feasible even in small dogs thus illustrating the possibility of human application. Here is another opera-

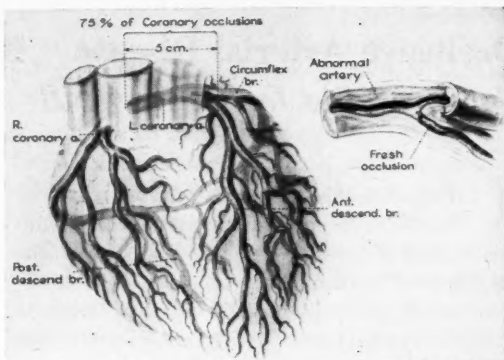


Fig. 1. Three-quarters of the serious or fatal coronary obstructions occur in the first two inches of the coronary arteries. This fact is an important circumstance prophesying future success in the removal of these obstructions by direct surgical methods.

tive photograph of an end-to-end left subclavian to left circumflex coronary arterial anastomosis in a dog utilizing a synthetic segment of artery constructed of Ivilon to bridge the gap between these two arteries. In conclusion, here is a third example in the dog of an end-to-end anastomosis between the left carotid artery and the left circumflex coronary artery. These operations have indicated to us beyond any reasonable doubt the feasibility of direct surgical procedures upon the coronary arteries either by endarterectomy or by resection of the diseased segments and their replacement by suitable grafts. The main barrier at the moment to human application is the lack of good diagnostic methods to show the exact site and extent of the coronary artery pathology preoperatively. This can be solved, probably best by more precise angiocardigraphic methods.

In conclusion I would like to emphasize that arteriosclerosis is one of the fields in which surgical advances are destined to contribute importantly to man's longevity. This is neither to overlook nor minimize the advances that can, must, and will come in other non-surgical forms of management or prevention of this disease. It is quite evident that the combined efforts of all fields of medicine, and in fact of anyone who has an idea, will be necessary before we will be in a position, as Oliver Wendell Holmes said, "to get ahold of nature and squeeze her until sweat breaks out over her brow and her sphincters are loosened."

Seventy-five per cent of all money raised in Minnesota for the Heart Fund remains in this state. Twenty-five per cent is sent to the American Heart Association, which in turn re-issues funds to all contributing states. American Heart Association has regularly returned more to Minnesota than it has received. Funds received

by the Minnesota Heart Association are allocated almost exclusively to research projects within the state devoted to diseases of the heart and blood vessels. MHA funds helped underwrite the research which made possible the development of the cross-circulation heart surgery technique.

## Occlusive Arterial Disease

### *Management by Use of Homografts*

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THE traditional concept that occlusive arterial disease of the extremities is associated with generalized obstruction has long held sway. The evidence of its inaccuracy has also been available, but we have only recently begun to recognize that all arteriosclerotic peripheral disease is not alike and that it is necessary to evaluate again this problem which through its very familiarity has lulled us into believing that all of its clinical and anatomical features are known.

We must evolve a new dynamic concept of the pathology and physiology of atherosclerotic disease which can recognize the manifold manifestations of the arteriosclerotic process and to separate from each other the different pathological variants. At the same time we must be able to correlate all of these features to understand better the sequence of events which occur under these different circumstances. Already much progress has been made, and most of these advances in our recent knowledge have come as a result of observations made at the clinical level by exacting detail in the physical examination, by arteriography and by observations at the operating room table rather than by examination of pathological material at autopsy.

From the practical point of view occlusive arterial disease may be classified into three primary categories: (1) major arterial occlusion; (2) primarily small vessel disease; (3) a mixed form in which both large arterial occlusion and small vessel obliteration co-exist.

It is essential in the treatment of any patient to determine into which of these groups he belongs and to determine the exact site and degree of the occlusion. If there is evidence of arteriolar disease, its role in the production of signs or symptoms must be evaluated.

When the disease primarily involves the large vessels the area of complete obliteration tends

to be segmental in a high percentage of cases. We have arbitrarily chosen to call all arteries proximal to the bifurcation of the popliteal artery large vessels because distal to this level direct surgical intervention is distinctly less successful at the present time than it is at higher levels, and in most cases the pathologic process which involves these vessels below this level also tends to involve the terminal arterial tree.

It is important to emphasize that high occlusions tend to be shorter than those at lower levels and that the majority of occlusions which begin above the level of the inguinal ligament end above the level of the femoral bifurcation. When major arterial obstruction is present in the absence of evidence of extensive small vessel disease, reconstruction of the major arterial trunk is the procedure of choice. Reconstruction of the major arterial obliterated segment may be extremely helpful even in the presence of small vessel disease, and the amount of benefit to be gained is dependent upon the extent of the small vessel obliteration and upon the amount of collateral which can be restored by reconstruction of the major trunk.

The natural history of the sequence of events which occur following a major segmental arterial occlusion have become more and more clear, and our current concept can be outlined briefly. It is interesting that most segmental occlusions tend to begin near or at a major bifurcation, implying that the hemodynamics of flow or anatomical structure may play a part. The process is usually one of gradual narrowing with subintimal thickening, ulceration and atheroma formation with progressive obliteration of the lumen. Ultimately, this ends in an episode of thrombosis whereby the remaining lumen is occluded. Usually, at the time that the total occlusion occurs the patient's symptoms markedly increase. This may be so sudden as to suggest embolic occlusion.

The pulsatile flow to the extremity is completely interrupted with the occlusive episode and the distal circulation then becomes completely collateral in type with a low systolic and a low pulse pressure. Proximal to the occlusion a blind

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segment now exists, and this undergoes a slow progressive thrombosis proximally to the point at which the next major branch arises. This process then usually becomes still slower and may even cease for a considerable period of time.

Distal to the occlusion there also continues a slow gradual thrombosis, again extending to the next major branch. If the vessel is still diseased at this level, the clot continues to accumulate on the distal thrombus until the next major collateral is obliterated. Relentlessly and slowly this progresses, picking off one by one the collateral blood supply to the distal extremity. The series of changes is so insidious that it may extend over a period of many years before the total arterial flow is so decreased that it jeopardizes the viability of the extremity.

On the other hand, if extensive disease is present in the major vessels, if there is co-existent small vessel disease to impair flow further or if poor collateral circulation is present, the thrombosis may extend extremely rapidly and lead to early gangrene. Similarly, the proximal extension of the thrombus, following the major arterial occlusion is variable and it may also gradually involve the proximal collateral circulation, or if the clot extends to the aorta it may then extend until it blocks the opposite iliac artery.

Thus, it is quite apparent that once a major segmental arterial occlusion has occurred a sequence of events is initiated which tends ultimately to lead to disability or destruction of the extremity, and this occurs principally as a result of the loss of the major forcible arterial pulsatile flow. Restoration of the major flow can greatly decrease the rate at which these and other changes of an obliterative nature will occur in the distal vessels which have varying amounts of disease.

For these reasons it is quite clear that arterial reconstruction with restoration of flow must be the treatment of choice in every situation in which it can be technically accomplished. These fundamental considerations are the basis of the rationale for the reconstructive approach to segmental arterial obstruction. Segmental obstructions may be long or short. Indeed, they may be treated when they extend from the level of the abdominal aorta to the knee, providing that a good patent channel is obtainable proximally and distally. The common sites for such chronic occlusions are: (1) in the abdominal aorta above

the bifurcation; (2) at the bifurcation of the aorta; (3) in the common iliac artery, involving the hypogastric artery; (4) at the level of the bifurcation of the common femoral; (5) in the adductor canal above the knee.

Occlusions of the abdominal aorta below the renal arteries without extension into the aortic bifurcation are not frequent. Occlusions of the aortic bifurcation may arise as obstruction of one common iliac artery initially with progression to involve the entire bifurcation or it may occur simultaneously on both sides. It is quite usual to see a unilateral iliac occlusion which on exploration shows considerable involvement of the mouth of the iliac artery on the opposite side. Occlusion of the iliac artery at the level of its bifurcation with involvement of the hypogastric artery is probably the most common of the intra-abdominal major arterial obstructions. It is interesting to point out that the hypogastric artery is frequently among the earliest vessels to show evidence of obstruction and obliteration.

In contrast to this when the bifurcation of the common femoral artery is involved it is more usual to see the preservation of the integrity of the deep femoral artery, and indeed, even when it is occluded by thrombosis which involves the common femoral artery the thrombus frequently does not extend far into the profunda femoris.

Adductor canal occlusion is one of the more common varieties which occur below the inguinal ligament. This may be of considerable length. When the obstruction exists at this level, it is more common to see extensive distal obliteration than when occlusion occurs at a higher level.

These segmental obliterative lesions may be attacked by endarterectomy, by replacement with homologous arterial segments, by replacement with autogenous venous segments or by the use of plastic arterial prostheses. Each of these methods has certain inherent advantages and disadvantages which we well recognize, and the method to be used will depend in part upon the individual operator's experience with each of the procedures and the location of the area of obstruction. This discussion will be confined to the use of preserved arterial homografts since our experience with these have covered the longest period of time. It should be understood, however, that this does not imply that we feel preserved arterial homografts are always the best choice nor that they will necessarily continue to

be the ideal method for arterial replacement in the future, for we are constantly seeking new and improved methods.

Homologous arterial segments can be preserved in a number of ways. Grafts may be taken aseptically, preserved by rapid freezing and storage at  $-70^{\circ}\text{C}$ ., or the rapid freezing process may be followed by dehydration and storage in a vacuum at room temperature. In the past several years it has not been necessary to take the grafts with aseptic precautions. They may be taken unsterilely and sterilized by irradiation with cathode ray emanations, beta-propio-lactone or ethylene oxide. We have adopted a simplified technique of securing the vessels without aseptic precautions at postmortem examination, sterilizing the grafts by immersion in ethylene oxide for 15 minutes, followed by rapid freezing, dehydration and storage in a high vacuum. The grafts are reconstituted at the time of use by immersion in saline solution. This method has given highly satisfactory results. It has been used in several hundred experimental grafts and in a very large number of clinical cases without evidence of graft failure due to methods of preservation.

Homografts preserved in this way have the advantage of ready availability and ease of storage at room temperature. Sealing in vacuum is helpful since one can determine immediately whether or not the seal of the tube has been broken. This can be accomplished by testing the vacuum with a high frequency spark coil. If the vacuum has been lost it must be presumed that the seal is no longer intact, and that the graft is therefore potentially contaminated and should be discarded. When such grafts are sealed in glass, they may be stored for periods of approximately two years following their processing without danger. It is of importance to realize however that all processes of dehydration are not the same, so that one must adopt a standard technique with rigid controls before one can expect to obtain uniform results. When the lyophilized grafts are reconstituted they regain their normal pliability and elasticity. This constitutes one of the major advantages of homografts. When one must replace a branching arterial segment such as an aortic bifurcation in which it is necessary to reconstruct the hypogastric and external iliac artery on each side, the adaptability of homologous grafts allows one a

great deal more freedom and ease of execution of the procedure than do some other forms of prostheses.

In any consideration of obliterative arterial disease involving the circulation to the lower extremities it is worthwhile to separate those lesions which occur in the vessels which lie within the abdomen and those which lie in the extremities themselves for the more proximal lesions are distinctly more favorable. Whether this is entirely related to the size of the vessels and the more difficult technical problems associated with the anastomosis of small arteries, whether there is a fundamental difference in the arteriosclerotic process in the different areas, whether it is a matter of the length of the graft necessary to replace the diseased segment or a combination of these factors is difficult to distinguish.

It is quite clear, however, that those lesions which lie in the aorta or in the iliac vessels alone and do not extend beyond the inguinal ligament have almost uniformly satisfactory results when the diseased segment has been replaced with homografts with end-to-end anastomoses. In contrast to this the results with replacement of vessels in the leg itself have been less reliable. These results have been changing constantly as more experience has been gained. The number of successful cases has markedly increased until at the present time with well selected cases one can expect approximately 80 per cent of the results to be good after two years of follow-up. The use of end-to-side anastomoses in selected instances has been helpful, particularly when one is dealing with the smaller vessels.

It would appear that many of the early poor results with removal of diseased arterial segments were due to excessively conservative resections. At first it was believed desirable to resect only a minimum of the artery and this in general was confined to the area of occlusion. This has more recently given way to the more radical concept in which it has been felt desirable to re-establish circulation at a point in which the vessel becomes relatively good and to remove as much of the diseased vessel as may be necessary to secure an arterial wall of as good quality as can be obtained above and below the site of the occlusion. It is also desirable to restore flow distal to those parts of the vessel which are partly obstructed. This may be accomplished in some cases by excision of all of this area or

in other cases by the use of end-to-side anastomoses which by-pass the area of obstruction.

A brief review of the common sites of occlusion together with the methods which are most readily applicable using preserved arterial homografts may summarize the current situation. Occlusion of the abdominal aorta without involvement of the aortic bifurcation is one of the less common obliterative lesions, but one will occasionally find this type of involvement without involvement of the aortic bifurcation, and the simple tubular aortic homograft may be used very satisfactorily to correct the situation. The aortic bifurcation thrombosis usually involves the proximal aortic segment for a considerable distance and may extend up as high as the renal arteries. The iliac involvement is variable and may not be the same on both sides. In a large number of individuals it is possible to use a bifurcation aortic graft for the single anastomosis proximally and one anastomosis in each common iliac artery just above its bifurcation. Very frequently however, on one side or the other the bifurcation of the iliac artery may be involved and an anastomosis must be accomplished between the external iliac artery and the hypogastric artery with the graft.

Occlusions of the common iliac artery are occasionally extremely short and a direct anastomosis of the segments may be accomplished after resection of the obstruction. Usually however, the area of thrombosis or of partial obstruction extends back to the aorta. If the opposite side is completely free of obstruction unilateral reconstruction is permissible. If there is evidence of serious disease on the other side however, it is optimal to use an aortic bifurcation graft with reconstruction of both sides. When unilateral reconstruction is attempted it is undesirable to attempt to use the stump of the iliac vessel if the arterial wall is of poor quality. In such cases an end-to-side anastomosis between the graft and aorta at a point above the aortic bifurcation where the aorta is less involved would appear to be the preferable procedure. The distal anastomosis can be made either end-to-end or end-to-side as the circumstances indicate.

When the obstruction extends distally beyond the pelvis and into the leg the proximal reconstructive procedures are the same as for those of the major vessels and the distal anastomosis can be made end-to-side with preservation of the

major collateral in the region of the inguinal ligament. When obstruction exists between the bifurcation of the femoral artery and the bifurcation of the popliteal artery, the various procedures are helpful. If the proximal obstruction is readily ascertainable just below the bifurcation of the common femoral artery, it is frequently simple and highly satisfactory to do an end-to-end anastomosis proximally. One may then isolate the popliteal artery or the femoral artery just above its entrance into the popliteal space, and if it is patent at this level, an end-to-side anastomosis can be accomplished without isolation of the intervening vessel. This is particularly helpful if large collaterals arise at the point at which the obstruction ends or if the vessel is quite small. End-to-end anastomoses have also been highly satisfactory in our hands and it would appear to be usually quite possible to obtain a distal stump of patent vessel without sacrificing collateral. This is particularly true if one bevels the anastomosis and thus avoids the circumferential suture in a single plane.

This brief résumé of some of the problems of obliterative arteriosclerotic disease of the arteries supplying the lower extremities brings into sharp focus the dynamic concept of reconstruction of major arterial continuity. It offers the possibility of restoration of adequate circulation and retardation of the progress of the disease in a very large group of patients.

When the obstruction lies above the inguinal ligament one can expect a successful outcome with long-term good results in approximately 90 per cent of the patients. When the obstruction lies within the leg itself and can be successfully treated by restoration of pulsatile arterial flow, good results can be expected in 70 to 80 per cent of the patients. The risk for the patient in such procedures is not great and is primarily related to the risk of concomitant arteriosclerosis involving other organs in relation to a major operative procedure. In our series of all types of operations for occlusive arterial disease, including the aorta and extremities the mortality rates are under 2 per cent. On the basis of present experience we can anticipate the benefits which are currently available in selected instances will be extended to larger groups of patients, and until the great problem of prevention of arteriosclerosis can be solved we will be able to restore more and more of these individuals to a useful life.

# Healing and Fate of Arterial Homografts

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RATHER than discuss Dr. Hufnagel's excellent presentation, I shall consider the general topic of the healing and fate of arterial homografts.\* My comments will be based upon studies of approximately 1,000 experimental vascular grafts carried out at the University of Washington School of Medicine and Walter Reed Army Medical Center over the course of the past five years.

From these studies has come the realization that to understand the healing of arterial grafts is to understand their fate. We have gained an understanding of the healing of arterial homografts which has given sufficient insight into their fate to be worthy of consideration.

So rarely do the cells of a homograft survive that for practical purposes our consideration may be directed entirely towards the fiber framework of the graft. The fate of this framework determines the fate of the graft. After implantation, living cells die. The basic histologic fate of homografts is independent of their state of viability at the time of implantation. The fibroblasts of adjacent host tissues proliferate and invade the homograft wall to varying depths and spread from the anastomotic site along its inner surface for short distances. The anastomotic junction is healed by the ingrowth of host fibroblasts from the aortic ends and from the surrounding tissues. Fibrous tissue from the anastomotic junction grows out to cover the inner surface of the adjacent 1 to 2 cm. of graft and 2 to 3 mm. of aorta. The extent to which the intima of the host aorta contributes to this process has not been determined. Some fibrillar elements taking the elastic tissue stain extend out from the aortic intima for 1 to 2 mm. along the inner surface of the fibrous tissue at the anastomotic site.

In most instances, the inner portion of the

homograft fiber framework becomes condensed to form an acellular, relatively inert, mass of foreign homologous protein which is impervious to the ingrowth of host tissue and remains so for periods of at least a year. Thus, only at and adjacent to the anastomoses (1 to 2 cm.) and to those sites where the fiber framework happens to remain pervious to the ingrowth of host tissue, or becomes so subsequently, does a layer of host tissue form along the inner surface of the homograft fiber framework. Accordingly, most homografts longer than 3 to 4 cm. are devoid centrally of an inner lining of host tissue. The condensed fiber framework of the homograft serves as an effective conduit for the passage of blood. It does not promote thrombosis. Apart from lack of perviousness, the homograft fiber framework is comparable to the plastic fiber frameworks currently being employed. However, the homograft fiber framework differs from the plastic fiber frameworks in that it is fabricated from better material in a superior manner. Because of this, the homograft is elastic, dependable, and durable. Plastic fiber frameworks have little elasticity and are not as adaptable as their homograft counterparts. The plastic fiber frameworks are best suited for bridging straight defects of large arteries where branches, angulation, and small caliber are not considerations.

In the early period following implantation, the strength of the graft resides in its homograft fiber framework. Subsequently, the autogenous fibrous tissue reaction about the homograft is sufficient of itself to serve as a suitable conduit. It is difficult to state how long the graft is dependent upon the integrity of the homograft fiber framework for its strength. As a generalization, three months is suggested. If the homograft fiber framework loses its continuity before the host tissues have been able to form an autogenous tube about it, rupture with hemorrhage occurs. If the continuity of the homograft fiber framework is lost before the host tissues have formed a *stable* autogenous tube about this framework, aneurysm formation with its attendant complications results. However, if the homograft

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\*Sauvage, L. R. and Wesolowski, S. A.: Healing and Fate of Arterial Grafts. *Surgery*: In press.

fiber framework continuity persists until the host tissues have formed a stable autogenous tube about this framework, a satisfactory conduit remains whether the homograft fiber framework subsequently loses its continuity or not.

Apart from rupture or aneurysm formation, the complications of thrombosis and degenerative change must be considered. Early thrombosis is due in the main to turbulent blood flow at the anastomotic site, which circumstance is largely the result of technical error or improper size of graft. Delayed thrombosis is largely related to the development of calcific changes in the graft wall. These changes occur in the inner condensed acellular portion of the homograft fiber framework. The reason for the development of these changes is obscure, but a probable cause is deficient nutrition in the vicinity of foreign protein. Calcific changes in the homograft wall of

themselves do not impair the ability of the graft to function as a conduit. However that such changes favor the development of delayed thrombosis or aneurysm formation seems certain. Longer clinical observation is required to ascertain the influence of calcific change upon ultimate graft fate.

As regards the use of homografts in the arteriosclerotic patient, these conduits with their attendant dangers are less liable to complications than is the rest of the arterial system of the patient. Accordingly, one may indorse their use in the arteriosclerotic patient with few reservations.

The results currently being obtained with plastic grafts are highly encouraging. However, for general use, the proper employment of appropriate homografts is still the recommended means for bridging arterial defects.

#### DISCUSSION—ARTERIOSCLEROSIS OF THE EXTREMITIES

(Continued from Page 901)

is a summary of his data. Sixty-two per cent of individuals who had healed myocardial infarction died of heart disease. Thus two-thirds died of conditions primarily related to their coronary disease. Approximately one-fifth died of congestive heart failure without further infarction, another one-fifth died of recurrent infarction, and one-fourth died a sudden death without failure, acute infarction or acute coronary occlusion. Again to focus our attention upon the therapeutic challenges, that of people dying *suddenly* is paramount, and assuming that this might be caused by ventricular fibrillation, then this is an avenue of investigation that must be further encouraged.

The therapeutic challenge of coronary disease I have thought might be epitomized by the titles of Churchill's volumes. This is a type of war, and the male sex is involved to a great extent. The *Gathering Storm* is the development of the atherosclerosis, and this may be present even when persons are in *Their Finest Hour*. The *Great Alliance* to help is the inherent capacity of the coronary circulation to develop collaterals, the subject's acceptance of restricted activities and the little help that the doctor may give. The *Hinge of Fate* is related to those factors that eventually should be elucidated, why some individuals live an active life with their disease for twenty years plus and others do not. The *Closing of the Ring* is the development of sudden coronary occlusions, and *Triumph and Tragedy* are the outcome of the acute destructive processes within the war-stricken myocardium.

HENRY I. RUSSEK: Everyone would agree with Dr. Burchell that the saving of even one patient out of every 100 stricken with acute myocardial infarction is

deserving of every therapeutic endeavor. I would like to point out, however, that while I strongly favor the use of anticoagulants in severe (poor risk) cases, the statistics presented by Dr. Burchell provide the weakest support for this form of treatment that I have thus far encountered. According to these figures, only one patient out of every 100 unselected cases of acute coronary occlusion dies of a thromboembolic complication. On the other hand, careful analysis has shown that anticoagulant therapy, even in the hands of the most competent investigators, is responsible for 1.7 deaths from hemorrhage in every 100 patients treated. In weighing these respective risks, it must also be realized that present-day therapy with anticoagulants does not achieve infallible prophylaxis. Consequently, while Dr. Burchell's objective is commendable, should we not ask ourselves whether or not we are merely substituting one mode of death for another? The answer can only be found by analyzing cases within a framework of prognostic categories based on clinical signs and symptoms.

Unless so considered, crude statistics may mask important facts. Thus, in patients with shock, congestive heart failure, arrhythmias and other poor prognostic signs, the incidence of fatal thromboembolism may be 5, 10 or more per 100 cases. Certainly, in such instances, the salvage possibilities from the administration of anticoagulants justifies the risk inherent in their use. In milder cases, on the other hand, thromboembolic deaths occur so infrequently that they are encountered in only a small fraction of 1 per cent of patients in this category. The use of anticoagulant therapy in this low-risk group therefore appears to be unwarranted. Certainly, all the evidence to date can lead to no other conclusion.

# Use of Greater Saphenous Vein Autografts in the Reconstruction of Segmental Arterial Occlusions

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WITH much of the current interest in arterial reconstruction being centered upon arterial homografts, plastic prostheses, thromboendarterectomy, and other similar techniques, it is felt that some mention should be made of techniques utilizing vein autograft segments. Nabatoff,<sup>1</sup> Julian<sup>2</sup>, Sako,<sup>3</sup> and others have shown that visceral veins, when placed as a graft to bridge a defect in an artery, have a tendency to dilate into aneurysmal formations. However, the greater saphenous vein is of adequate size, has a muscular media and, as demonstrated by Julian,<sup>2</sup> has the strength to withstand arterial pressures. It is fortuitous that the greater saphenous vein is almost universally available for the sacrifice of its normal function for other purposes.

TABLE I. SAPHENOUS VEIN AUTOGRAPHS

Arterial Segment	Result
1. Abdominal aneurysm	Failure
2. Femoral aneurysm	Failure
3. Abdominal aneurysm with iliac artery occlusion	Excellent
4. External iliac	Excellent
5. Superficial femoral stenosis	Thrombosed vein
6. Superficial femoral occlusion	Excellent
7. Superficial femoral occlusion	Excellent
8. Superficial femoral occlusion	Excellent

It is felt that the techniques which utilize the replacement of an arterial segment which is occluded, by "in lying" methods, present an undue hazard to the extremity when used in distal arterial beds. Small collateral vessels must be sacrificed in the exposure and resection of the occluded arterial segment; thus, if the graft should fail, the extremity is often sacrificed. Linton<sup>4</sup> has described a technique whereby occluded arterial segments may be by-passed, by an end-to-side anastomosis of an arterial homograft above

and below the occluded portion of the artery, thus obviating this difficulty. In our clinic, the possession of a store of arterial homografts has proven extremely difficult, and as such, we have



Fig. 1. Femoral angiogram of a femoral aneurysm showing contrast media filling only the distal end of a vein graft around the aneurysm. The proximal end of the graft was compressed by enlargement of the aneurysm. Case 2, Table I.

preferred to evaluate this by-pass procedure by using the ready supply of greater saphenous vein autografts.

In the University of Minnesota clinics, patients with symptoms of intermittent claudication, with absent peripheral pulses, are evaluated with arteriographic studies. If segmental occlusive dis-

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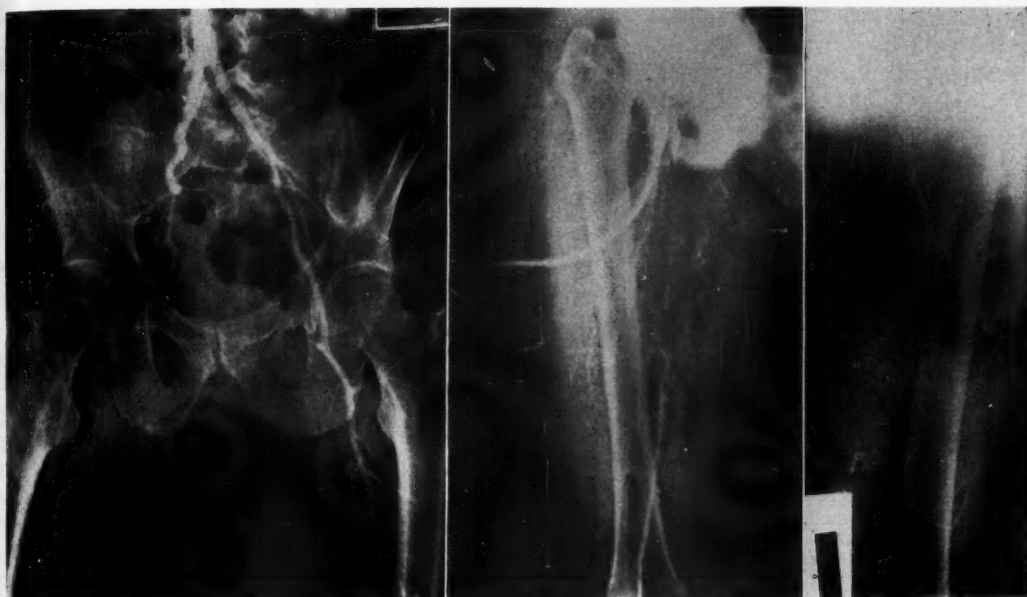


Fig. 2. (left) Aortogram showing segmental occlusion of the external iliac artery, with good filling of the femoral artery below the inguinal ligament. Case 4, Table I.

Fig. 3. (center) Femoral angiogram showing occlusion of the superficial femoral artery in Hunter's canal. Case 6, Table I.

Fig. 4. (right) Femoral angiogram showing occlusion of the superficial femoral artery with good filling below Hunter's canal. Case 7, Table I.

case is found above the popliteal artery, the patient is considered a candidate for an arterial reconstruction.

### Technique

The patient is placed upon the operating table in the supine position, and a small sand bag inserted under the opposite hip when the popliteal space is to be entered. Using the technique described by McPheeter,<sup>5</sup> the saphenofemoral junction of the greater saphenous vein is dissected and all branches ligated and severed. The vein is then removed, using an external Mayo vein stripper, and all branches ligated as they are encountered. Fortunately, there are few branches to this vein above the knee, and the segment of vein from the groin to the knee is usually of sufficient length. The vein is then washed with saline to remove all blood and clots.

If the occluded arterial segment is intra-abdominal, a mid-line abdominal incision is satisfactory. With external iliac artery occlusion, we prefer a retroperitoneal approach. In occlusions of the superficial femoral artery the original incision at the sapheno-femoral junction is adequate to

expose the femoral artery, and by rotating the table slightly, a curved incision at the medial edge of the popliteal space will expose the popliteal artery distal to Hunter's canal.

Heparin, 50 mg. is injected into the artery at its proximal exposure, just prior to placing the occlusive clamps during the arteriotomy. An elliptical arteriotomy is made, and with a beveled terminal end to the vein graft, an end to side anastomosis is carried out, using 5-0 arterial suture. The distal end of the vein must be anastomosed to the proximal arteriotomy site, and the proximal end of the vein anastomosed to the distal arteriotomy, to prevent the interference of blood passage through the graft by the venous valves.

If the graft is to by-pass the superficial femoral artery, we have found it advantageous to replace, but reverse, the vein in its original site, to the knee, then anterior and beneath the vastus medialis muscle, into the popliteal space.

It is further felt to be advantageous to by-pass a segment of artery from the junction of a large vessel above the occlusion, to a similar junction below the lesion. Thus, for external iliac artery

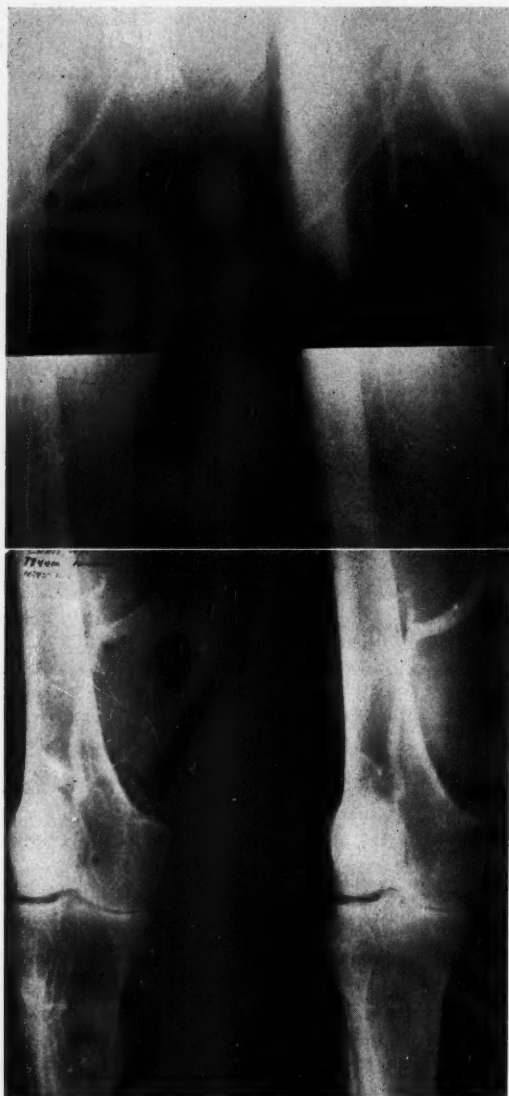


Fig. 5. Femoral angiogram, taken three months after insertion of the graft, shows filling of the vein graft and distal vascular bed, Case 7, Table I. Note the dilatation of the graft in the area of the inverted valves.

occlusion, we graft from the origin of the hypogastric and the external iliac arteries, to the origin of the deep and superficial femoral arteries. At these spots, the lumen of the artery is at its greatest, and the anastomosis may be easily carried out. Unfortunately, in the popliteal space, there are no such large branches distal to Hunter's canal.

## Results

Eight procedures utilizing the above technique have been carried out (Table I). Five of these were occlusive disease, and three were attempts to bridge around aneurysms prior to their resection or with occlusion distal to the aneurysm. In one instance, the vein was found to be thrombosed when it was removed, and thus proved unsatisfactory for a graft. In the remaining seven instances, the grafts functioned well at the time of surgery.

In two of the three instances in which the graft was used to bridge around aneurysms, the procedure was unsatisfactory. In one instance, the aneurysm enlarged, to occlude the graft (Fig. 1). In the second, the graft was exposed at a second operation in an attempt to remove the lesion, and the proximal anastomosis was found occluded due to extension of clot from within the aneurysm. In the third instance the graft functioned satisfactorily for two years with complete relief of claudication during this period until the patient expired from other causes.

In the four instances where the grafts were bridged about blocked segments of artery, and were satisfactory at the time of surgery, they have remained functioning to the present time, although the follow-up period has been short (Figs. 2, 3 and 4).

Patients have been evaluated with pre-operative and post-operative plethysmographic studies using the technique of Windsor.<sup>6</sup> In all instances, there has been a marked change in the digital pulse volume, greatly exceeding that expected by a sympathectomy. In no instance in this series, was a sympathectomy done concomitantly with the vein graft. In all these patients, there has been relief of claudication, and in the one patient with rest pain, there has been complete relief of symptoms. In another instance, the patient had suffered from a large chronic ischemic ulcer on the anterior tibial area, for three years prior to surgery, which was refractory to conservative therapy. During the ten-day postoperative hospital stay the ulcer epithelized without special therapy, and has remained healed to this time.

## Discussion

It is felt that this by-pass type of arterial reconstruction is of value for several reasons.

1. There is no sacrifice of small collateral ves-

sels as in methods requiring the removal of the diseased arterial segment.

2. In the event of failure of the graft by early or late thrombosis, the preoperative blood supply to the limb has not been impaired.

3. The operative procedure may be done through a small incision, with little blood loss, safely, even in a poor risk patient.

The simplicity of the procedure described is further exemplified since there is no need for a store of arterial homografts. Furthermore, there is no need for special instruments or procedures to make and develop plastic arterial prosthesis. The pliability of the vein wall makes it available to place across movable joints and for use in the extremity. In reality, the above technique is not an artificial reconstruction of an occluded artery, but is instead, the surgeon's attempt to increase the efficiency of nature's method of healing this lesion, by the development of a large collateral channel around the occlusion.

### Summary

A technique of reconstruction of the arterial

bed in segmental occlusive vascular disease, by the use of a by-pass saphenous vein autograft, has been described. The results of early follow-up in eight patients is presented. It is suggested that this technique may be used without some of the hazard of other procedures, and without the necessity of an arterial homograft bank or the use of non-vital prostheses.

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Although the Minnesota Heart Association places its greatest emphasis by far on heart disease research, it is also concerned with education and community service. Currently, the chief community service project is the Heart Council, to which MHA turns part of its attention when the annual Heart Fund drive is over.

MHA is attempting to organize permanent Heart Councils in most of Minnesota's major cities. Although the program is very young, several Heart Councils are already functioning within the state.

Composed of lay and professional persons interested in heart disease problems, the Heart Council's basic function is to inform the public about heart disease. This information program is not built upon creating fear in the minds of persons—but rather on informing them of the new hope for afflicted hearts.

Methods of informing the public are as varied as the ingenuity of individual Heart Council members.

Most common are films, speakers, the press, radio, and television. Other popular means are Health Days, state and county fairs, and displays.

Twelve councils now exist in Minnesota, and a thirteenth is being formed. Minnesota Heart Association's ultimate goal is the establishment of Heart Councils in each and every Minnesota community. Funds for the activities of the Heart Councils are included in the budget of MHA. Minor expenses necessary to carrying out a Heart Council program are underwritten by the state organization. It is an investment well worth making, in the opinion of MHA's Board of Directors.

It is not intended that the Heart Council be used as a tool in the annual fund-raising campaign of the Minnesota Heart Association. Although its activities will benefit the Heart Fund drive because of increased public awareness, the council's main job is still educational. Through education will come increased understanding of the problem of heart disease.

# Surgical Treatment of Aneurysms of Arteriosclerotic Origin

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ARTERIOSCLEROSIS is so frequently associated with dilatation and elongation that it is not surprising that discrete localized aneurysms not infrequently occur. More surprising and difficult to explain is the localization of these discrete aneurysms to specific regions. Aneurysms of arteriosclerotic origin may occur in any region of the body, the arm, head, thorax, lower extremity, or abdomen, but of peripheral vessels the popliteal is most commonly affected, and of the aorta itself, the region of the terminal aorta. Aneurysms of the peripheral arterial system present somewhat different problems from those of the aorta itself, and these two types of lesions will be considered separately. Cerebral aneurysms constitute a totally different condition and will not be considered.

## Peripheral Aneurysms

Peripheral arteriosclerotic aneurysms may occur in almost any vessel, but since they are most common in the popliteal artery and since treatment of popliteal aneurysm is representative, this lesion will be specifically considered.

Little is known why the popliteal fossa is the site of predilection for arteriosclerotic aneurysms, though the most commonly given explanation is that of repeated flexion. Once dilatation of the artery begins, physical factors are such as to encourage enlargement of the aneurysm. Stress on the arterial wall is directly proportional to the diameter of the vessel so that as the diameter doubles the tendency for rupture doubles, and the stage is set for progressive enlargement. Males are more commonly affected, and frequently the aneurysm is bilateral. Symptoms are of two types. The mass in the popliteal fossa may cause pain and discomfort in this region, or

ischemia of the lower leg may occur as manifested by ulceration, ischemic neuritis or intermittent claudication with pain in the calf. In some instances acute disability may arise from arterial occlusion.

In the past it has not been considered a particularly dangerous lesion and most surgeons have felt the danger of operation to be greater than the risk of the aneurysm itself. Hence in the absence of symptoms treatment was often not advised. A review of 100 cases by Gifford, Hines, and Janes at the Mayo Clinic, however, showed that untreated popliteal aneurysms are associated with a high incidence of complications (sixty-two of their 100 cases) in the form of arterial occlusion, rupture, or pressure on veins and nerves. Complications in 23.4 per cent of the aneurysms treated without operation led to amputation of the limb which harbored them. On the other hand, only 7.7 per cent, or two of twenty-six patients, treated operatively required amputation. Both of these aneurysms were in the early postoperative period in patients whose extremities were in peril before operation.

This observation led these authors to advise an aggressive surgical approach to popliteal aneurysms, and their preferred method of treatment at that time was sympathectomy and extirpation of the aneurysm. This can usually be done with impunity although increase in the signs of peripheral ischemia may be seen. Because of this we have recently preferred to treat this as well as aneurysms of most major vessels by excision and restoration of arterial continuity by use of a graft (Fig. 1). Our first such lesion was treated by autogenous vein graft, taken from the deep popliteal vein, after it was apparent that the saphenous would not be adequate.

More recently we have had available frozen-dried arterial homografts and have found these to be quite satisfactory in three instances for popliteal aneurysm. The fate of homografts in the peripheral arterial system does not appear

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## ANEURYSMS OF ARTERIOSCLEROTIC ORIGIN—BAHNSON

to be as bright as in the larger vessels, the aorta and the iliac, but if occlusion occurs it is more apt to be of slow progression and concurrent with the development of collateral circulation. This

clinically, as well as pathologically, between arteriosclerotic aneurysms and the other major types of aortic aneurysms, principally those due to syphilis. Syphilitic aneurysms are more fre-



Fig. 1. Arteriogram and resected specimen from patient with bilateral popliteal aneurysms. A graft was inserted with maintenance of pulses and circulation. Patient initially seen with gangrene of contralateral limb from complication of untreated aneurysm.

then seems to be a decided advantage over simple abrupt ligation of the popliteal artery. Our three patients with four popliteal homografts continue to do satisfactorily after periods of twenty-five, fifteen and eleven months since operation. Each of these patients had open aneurysms and was operated upon in the absence of significant symptoms. When complete thrombosis has occurred I would perform an operation only for symptoms. If there is no evidence of distal ischemia, excision alone is indicated. When ischemia is present a graft should be used if possible and the lesion treated as any other such arterial occlusion.

### Aortic Aneurysm

Aortic aneurysms due to arteriosclerosis are, with surprising uniformity, localized to the terminal abdominal aorta below the origin of the renal arteries. There is a striking difference



Fig. 2. Aortogram showing lumen of contrast filled aortic aneurysm. A better index of size is the calcified rim adjacent to the gas filled colon.

quently, although not invariably, saccular, most common on the ascending aorta and aortic arch, seen in younger individuals, between forty and sixty, and more frequently associated with pain or pressure on adjacent structures. Arteriosclerotic aneurysms are usually located below the renal arteries, are usually fusiform, more commonly seen in older individuals and predominantly males, often associated with pain but only uncommonly with disturbance of function of the adjacent abdominal viscera. These aneurysms are becoming increasingly common in the experience of most, as was shown by Maniglia and Gregory.

The localization to the distal aorta is a fortuitous and fortunate feature although the reason is unknown, other than that arteriosclerosis is most prominent in this region. From physical examination, the question often arises as to whether an aneurysm disappearing under the costal margin does not extend above the renal



Fig. 3. Adjacent areas of the aorta and iliac vessels have been mobilized for occlusion with little dissection of the aneurysm.



Fig. 4. After occlusion of the entering vessels the aorta adjacent to the aneurysm can be divided and the aneurysm lifted from its bed. This greatly facilitates dissection.



Fig. 5. Arterial homograft sutured in place to restore arterial continuity.

arteries. This can easily be reconciled with the known localization below them when one realizes that the bifurcation of the aorta is often immediately behind or even above the umbilicus and the renal arteries arise behind the xiphoid. Of the fifty-four abdominal aneurysms that we have seen in the past three years only three have extended above the renal arteries, and in one of these syphilis was also an etiological agent. This is not to say that arteriosclerotic aneurysms do not occur above the kidneys, as discussion later will show, but that when there is a discrete aneurysm in the abdominal aorta, the chances of it being localized below the renal arteries are very great.

The most frequent complaint of patients with an abdominal aortic aneurysm is the aneurysm itself, often found by physicians during routine examination or evaluation for other conditions. Some patients will complain of fullness, particularly after meals, pulsation, nausea, or other nonspecific gastrointestinal disturbances. Pain is not uncommon, and has been present at one time or another in about half of our patients and of such severity as to require opiates or the loss of weight. The severity of the pain is frequently variable and in itself is probably not a good prognostic sign. Pain, when present, has not been

of a characteristic type or distribution. It is usually felt in the abdomen, often in the back, and frequently associated with tenderness of the mass itself.

We performed aortography on all of the earlier cases of abdominal aneurysm but now use it only when disease is obviously widespread, as suggested by a large thoracic aorta, when we cannot be certain clinically that the pulsating abdominal mass is not simply a slightly dilated and tortuous aorta, or when absence of pulses suggests an additional iliac stenosis. The procedure is not without danger, as we have seen sizable retroperitoneal hemorrhage sufficient to cause shock, and paraplegia from a probable thrombosis of the anterior spinal artery. Much of the lumen of the aneurysm fills with clot, and the channel filled with contrast material may be nearly normal size. The calcified rim is a better radiological index of size (Fig. 2).

The prognosis of the patient without treatment of his aneurysm is not bright. The best available data, I believe, are those of Estes of the Mayo Clinic, and from these one can estimate that about one out of five patients with arteriosclerotic aneurysms will rupture the aneurysm within one year and one-half within three to five years. It was easy for me to believe that the prognosis is

even worse than this when I discovered that of the twelve patients seen in the last eighteen months whom, for one reason or another, operation was advised but not accepted, at least three are now dead because of rupture of the aneurysm. In addition one patient had a rupture and death the morning he was to be admitted to the hospital for examination.

Many forms of treatment have been used and advocated in the past such as cellophane wrapping, wiring, ligation, and aneurysmorrhaphy. None of these is associated with a sufficiently low operative risk and sufficient therapeutic benefit to justify operative treatment. The ideal treatment, and the method we are employing exclusively, is excision of the aneurysm with reconstruction by use of a graft. Wide exposure must be obtained, and we usually open the midline from symphysis to xiphoid. The aneurysm is usually densely adherent to the adjacent structures, but one may readily isolate the aorta above, between the renal arteries and the aneurysm, and the iliac arteries may be mobilized distally (Fig. 3). When these areas are occluded, bleeding is well controlled, as frequently the lumbar and inferior mesenteric arteries are thrombosed. The aneurysm can be lifted and dissected out of its bed (Fig. 4), though occasionally adherence to the adjacent vena cava is so dense that a portion of the aneurysm should be left attached to the vein. Restoration of arterial continuity can be obtained by use of an arterial homograft and anastomoses are done with standard cardiovascular techniques (Fig. 5). Grafts which we have employed have been either frozen-dried arterial homografts or, more recently, nylon bifurcation grafts. We have had no evident difficulty from occlusion of the aorta, although the time of occlusion has varied up to 150 minutes.

Since February, 1953, we have operated upon forty patients with abdominal aortic aneurysms. Thirty-one, or about three-fourths, of these are now alive and as active as their age allows. Four patients died for whom emergency excision was employed after vigorous resuscitation for a ruptured aneurysm. Three patients died either during or soon after an elective operation, which makes the operative mortality for an elective excision about 10 per cent. Two patients died four and six months following operation of coronary artery disease. These last two patients and one other lost a lower extremity because of ischemia.

Embarrassment to the distal circulation was most likely due to dislodgment of emboli which form in the occluded vessels during excision or of thrombus from the aneurysm itself. Use of heparin and care in mobilization of the aneurysm has eliminated this complication in more recent cases. We have also removed several emboli from the distal circulation following operation. In one individual, extreme blanching of the leg occurred during operation and continued, with slow improvement over the subsequent several days. Later a pulse could be felt which was as vigorous as that felt prior to operation, and it was believed that almost certainly spasm alone was the cause of the difficulty. Spasm has not apparently been a problem in other patients.

Arteriosclerotic aneurysms in the more proximal aorta are less apt to be well localized, although we have seen discrete saccular aneurysms of the lower thoracic aorta due to arteriosclerosis alone, as far as can be determined by available means (Fig. 6). Such saccular aneurysms are treated by excision and homograft during a brief period of aortic occlusion. Duration of aortic occlusion at this level must be as brief as possible, probably no more than thirty minutes.

We have seen two patients with long diffuse dilations of the thoracic aorta, one thirty-one and the other forty-six years old. Syphilis was almost certainly excluded as an etiological agent in both individuals. In the first patient (Fig. 7) the aneurysm extended from the origin of the left subclavian artery through the region of the renal arteries. An attempt was made to excise this with aneurysmorrhaphy, an internal shunt and massive transfusions, but the effort was unsuccessful as the patient died the following day of continued shock and with a paraplegia. A second patient is being observed and, if the aneurysm continues to enlarge, will be treated probably by a staged excision.

I have borrowed from the work of DeBakey, Cooley, and Creech, a discussion of dissecting aneurysms of the aorta. These aneurysms have a particularly poor prognosis and no treatment in the past has been effective in prolonging survival and preventing further dissection and ultimate rupture. A double lumen is frequently present, often with a saccular component at some area of the second channel. This has been attacked by excision of the saccular component, if one is present, or if not, by interruption of the

## ANEURYSMS OF ARTERIOSCLEROTIC ORIGIN—BAHNSON

aorta and closure of one lumen of the aorta. In some instances the site of initial dissection has been excised and the single proximal channel anastomosed to the distal double segment, a sin-

associated with irreversible damage to the abdominal viscera, particularly the liver and kidney. More proximal to this interruption of the circulation to the spinal cord is apt to be asso-

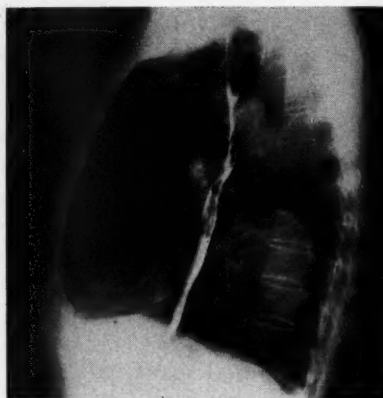


Fig. 6. Roentgenogram showing uncommon saccular arteriosclerotic aortic aneurysm just above the diaphragm.



Fig. 7. Extensive aneurysm in a thirty-one-year-old man extending from the aortic arch through the upper abdominal aorta. This was apparently due to arteriosclerosis.

gle distal lumen being made with the anastomosis. This procedure is of only relatively recent development and ultimate results remain to be determined. To date six patients have been operated upon. Five of the six patients remain well, and one died in the early postoperative period of ventricular fibrillation perhaps related to the use of hypothermia.

In instances where the aorta must be interrupted, as is true of almost all aortic aneurysms due to arteriosclerosis, hypothermia has been suggested and used by some in order to lessen the damage to the central nervous system during the period of occlusion. We have not believed this to be indicated in patients we have treated. As mentioned above, we have no difficulty with occlusion of the terminal aorta for periods up to two and a half hours, and, as far as I know, no difficulty due to this alone has been encountered by others. Proximal to the origin of the abdominal visceral vessels a much shorter period of time, exact duration of which is unknown, is

ciated with paraplegia. Especially in the age group in which arteriosclerotic aneurysms occur, the risk of hypothermia seems great, and we have preferred either to use an aortic shunt or more commonly to remove the aneurysm and reanastomose the aorta as quickly as possible. Bypass shunt grafts, as temporary or permanent substitutes for long and extensive aneurysms of the thoracic aorta, have been successfully used for non-arteriosclerotic aneurysms, but the full possibilities of this method remain to be determined.

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## Plastic Replacement of Diseased Arterial Segments

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CORRECTIVE surgery of diseased arterial segments entails methods for reopening or by-passing occluded and stenotic arteries and the obliteration or excision of aneurysms. For the former, two methods are available—thromboendarterectomy and the interpolation of grafts. Aneurysms of peripheral arteries can be treated by methods which involve ligation of the affected artery, but whenever a main-stem artery is affected it is highly desirable to maintain or restore its continuity. Certain saccular aneurysms of peripheral arteries and of the aorta can be excised with closure of the mouth of the sac by lateral suture. Occasionally, a peripheral aneurysm can be extirpated with approximation of the ends of the divided artery by end-to-end suture, and, rarely, this is possible in the case of an aortic aneurysm. Generally, however, a graft must be used. The need for grafts is, therefore, great.

For peripheral artery substitution autogenous veins may be employed with success. Not infrequently another type of graft is preferable for replacement of a peripheral artery and this is always true in the case of the aorta. Experimental observations from a number of laboratories suggest that venous transplants to the aorta would not be safe even if a suitable segment of autogenous vein were available, and there are no expendable appropriate veins. Arterial homografts have proved generally reliable up to the present time. To be sure, not all homografts have continued to function without complications,<sup>1,2</sup> and I know of several late disruptions which are not reported in the literature. Their chief disadvantage is the difficulty of acquiring them in sufficient numbers to meet the demand for their use. Over a period

of years various possible substitutes have been investigated. In general, permanent intubation of arteries with rigid tubes of glass, plastics, and various metals did not prove successful. There was a high incidence of thrombosis and when they were used to replace defects in the aorta the encircling ligatures all too often resulted in necrosis of the aortic wall with fatal hemorrhage. Hufnagel and Gillespie<sup>3</sup> found, however, that tubes of highly polished methyl methacrylate would remain patent and that ischemic necrosis of the aortic wall could be obviated by using the principle of multiple point fixation. Using this method, Hufnagel and his colleagues<sup>4</sup> demonstrated that short, rigid, plastic, valve-containing tubes could be employed successfully in patients with aortic insufficiency. Obviously, the ideal plastic for general arterial substitution would be an inexpensive, readily available material obtainable in, or made without difficulty into, tubes of various sizes and shapes, sterilizable by ordinary operating room methods, pliable and easily sutured to the artery by regular vascular suture techniques. It should further be non-reactive, relatively impervious to blood, and have such properties that it would become well incorporated into the new vessel formed about it by the host. The first contribution of this sort was the demonstration by Voorhees, Jaretzki and Blakemore<sup>5</sup> that short tubes made of Vinyon-N cloth could be sutured to the divided ends of the aorta, served well as a conduit and became covered by a new, smoothly lined fibrous aorta. My interest and that of my associates in plastic fabrics as possible arterial grafts arose through the use of a finely woven nylon cloth\* in the repair of atrial and ventricular septal defects. It was tolerated in the chambers of the heart and became firmly united with the septum and covered with a smooth endothelial-like membrane.

\*This cloth has 277 by 240 strands per square inch, obtained from Stehli Company, Inc., 1372 Broadway, New York, —241 F nylon fabric.

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When it was first used to bridge aortic defects in dogs, this nylon fabric proved so permeable that great blood loss often occurred through the graft. For this reason, various methods for ren-

The grafts soon became incorporated in a new fibrous aorta with a relatively smooth inner lining composed of cells which looked like endothelial cells (Fig. 2). The outer and innercoats were



Fig. 1. Aortogram showing nylon-polythene nylon graft, 7.7 cm. in length and 230 days old. (From Shumacker, H. B., Jr., et al: *Surgery*, 37:80, 1955.)

dering it more impermeable were investigated. The fusing together, by ironing with an electric iron set to "wool," of two layers of the nylon with a thin sheet of polythene\*\* in between served satisfactorily. In the initial study<sup>6</sup> seventeen grafts 1 cm. in diameter and varying in length from 5 to 10.8 cm. were observed for periods of from two to 310 days. All but one remained patent. The incidence of thrombosis was higher, however, when tubes 0.6 and 0.8 cm. in diameter were used. Of ten such grafts varying in length from 4.8 to 7.5 cm., observed for from one to 162 days, six remained patent and four clotted. For grafts of larger size the material seemed quite good. It was pliable and easily sutured to the ends of the aorta. Little or no blood loss occurred. The aortograms looked good (Fig. 1).

\*\*Obtained from the Clay-Adams Company, Inc., 308 W. Washington Street, Chicago, PE 2600 Polyethylene film, 0.0015 thickness.

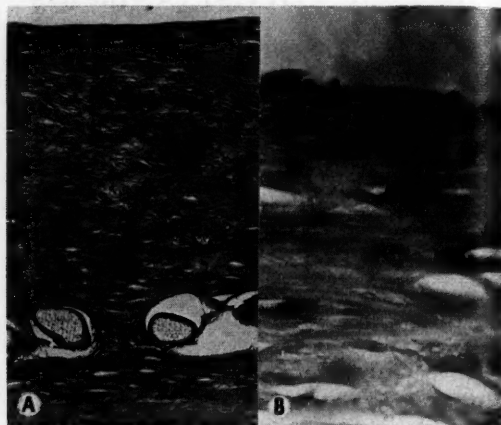


Fig. 2. Photomicrographs of inner portion of graft in dog 618. Age of graft 310 days. A—low power showing growth of fibrous tissue between filaments of nylon. B—high power, showing endothelial or endothelial-like cells lining graft.

intimately adherent to the plastic tube and fibrous tissue grew into the pores of the nylon. Ninety-four per cent of the larger grafts remained patent. During the course of this study, it was necessary to use similar grafts for human aortic replacement because of lack of availability of homografts.<sup>7</sup> They seemed to work well. Concurrently, the same nylon cloth coated with a thin film of methyl methacrylate was investigated. Again, the incidence of patency was high with grafts 1 cm. (92 per cent) and lower with grafts 0.6 and 0.8 cm. in diameter (68 per cent). These grafts, however, were not as satisfactory as the others for in a number of instances narrowing occurred as the result of a thrombus laid down between the plastic tube and the outer fibrous coat.

My associates and I<sup>8,9</sup> have subsequently undertaken a comparative study of a variety of plastics and sufficient experience has been obtained to permit an evaluation of four types of plastic grafts and to compare them with freeze-dried aortic homografts.<sup>†</sup>

†The aortic homografts were removed from donor animals without aseptic precautions, cleaned of all fatty areolar tissue, covered with liquid ethylene oxide for one hour, frozen quickly in Pyrex tubes immersed in dry ice-acetone bath, lyophilized, and stored in sealed tubes filled with nitrogen.

# PLASTIC REPLACEMENT OF ARTERIAL SEGMENTS—SHUMACKER

TABLE I. RESULTS WITH HOMOGRAFTS AND A VARIETY OF PLASTIC GRAFTS

Age of Graft in Days	Excellent	Good	Satisfactory	Poor	Dog Alive with Good Pulses
<b>Homografts</b>					
0-29	3	0	0	1	0
30-149	4	1	0	0	0
150-249	3	1	0	0	0
250-349	1	0	1	0	2
350-400	0	0	0	0	2
<b>Nylon Filter Fabric</b>					
0-29	7	2	0	0	0
30-149	4	3	1	1	2
150-249	0	4	1	0	9
250-349	1	0	0	0	2
<b>Braided Nylon Tubes Treated with Formic Acid and Silicone</b>					
0-29	2	0	1	1	0
30-149	3	0	0	0	0
150-249	0	0	0	0	9
<b>Two Layers of Nylon Fused with One Layer of Polythene</b>					
0-29	2	1	0	3	0
30-149	1	1	0	0	0
150-249	1	1	0	0	2
250-349	0	0	0	0	2
350-400	0	0	0	0	3
<b>One Layer of Nylon Fused with One Layer of Polythene</b>					
0-29	4	1	0	2	0
30-149	0	2	0	1	0
150-249	1	0	3	0	0
250-349	0	0	0	0	3
350-400	0	0	0	0	3
<b>Vinyon-N</b>					
0-29	0	0	1	5	0
30-149	2	1	1	0	0
150-249	3	0	0	1	0
250-349	0	0	0	0	1
350-400	0	0	0	0	1

One is a nylon filter fabric,<sup>‡</sup> one the previously described material composed of two layers of thin nylon and one of polythene fused together, one commercially fused§ single layers of the same nylon cloth and polythene film, and one a Vinyon-N cloth similar to that used by Vorhees, Jaretzki and Blackmore.<sup>††</sup> All plastic grafts were sewn together by machine with a fine needle and fine nylon thread, 25 stitches per inch. Some, but not all, of the nylon filter fabric was washed beforehand in Tide. The rest of the plastics were unwashed. The Vinyon-N grafts were boiled in

<sup>‡</sup>This is an off balance taffeta, constructed of multifilament twisted yarn strands with a warp count of 232 and a filling count of 96. It is 70 denier, high tenacity nylon with 36 turns per square inch. After autoclaving, it has such a resistance that a pressure equivalent to from 4 to 5 inches of water will cause it to pass 20 C.F.M. per square foot of air. The tubular grafts were fashioned by cutting the material on the bias so the strands of the warp were at a 45° angle to the long axis of the graft. HT-5F nylon filter fabric. Equipment Development Company, Inc., 368 Bloomfield Ave., Montclair, N. J.

<sup>§</sup>Obtained through the courtesy of Dr. C. E. Iron, Ben-Mont Papers, Inc., Bennington, Vermont.

<sup>††</sup>Supplied by Mr. T. P. Mulligan, Carbide and Carbon Chemicals Company, a division of Union Carbide and Carbon Corp., 30 E. 42nd St., New York 17, N. Y.

water for fifteen minutes. The other plastic tubes were autoclaved at 250° F. and at 20 pounds pressure for ten minutes. The freeze-dried homografts were reconstituted by soaking them in normal saline solution containing streptomycin and penicillin for one hour.

All the grafts were 5.4 cm. in length and all the plastic tubes were 0.78 cm. in diameter. They were sutured into thoracic aortic defects of dogs following excision of a 5 cm. segment under moderate hypothermia. An everting mattress suture of 5 zero silk was used. Only in the case of the Vinyon-N grafts was a cuff turned back at each end of the tube.

Some observations were also made with the braided nylon seamless tubes of Edwards and Tapp.<sup>10††</sup> This study is similar but not entirely comparable to that of grafts made from the other plastics. These tubes were of two sizes, approximately 0.4 and 0.6 cm. in diameter. They, too, were 5.4 cm. in length. They were sutured to the aorta with a continuous plain over-and-over stitch. This series of grafts was not studied over as long a period of time as the others.

The results of these investigations are tabulated in Table I. Grafts are classified as excellent when they were found to be widely patent with a thin, smooth lining and were without external constriction or clots. They were considered good when they were widely patent with an essentially smooth lining, with minimal erosion or degenerative changes, and without external constriction but with minimal external clots in some cases. If the pathway through the graft was narrowed and yet served as a satisfactory conduit or if the inner coat was roughened due to a mural thrombus or excessive intraluminal fibrinous reaction or if there was some external constriction from a large clot or fibrous reaction, the result was classified as satisfactory. It was considered poor if it failed as a conduit either from exsanguination through the graft, disruption, or an occluding thrombus. Four animals are excluded from consideration because the unsatisfactory result seemed clearly the consequence of a technical error.

Detailed data are listed in the first table. In Table II the results for each group are summarized.

<sup>††</sup>These braided tubes have a large porosity. They were treated with formic acid to solve the problem of easy frayability, crimped in an accordion-like manner to permit bending without wrinkling, and siliconed to prevent blood loss through the wall of the graft.

# PLASTIC REPLACEMENT OF ARTERIAL SEGMENTS—SHUMACKER

TABLE II. RESULTS WITH HOMOGRAFTS AND A VARIETY OF PLASTIC GRAFTS FROM STUDY AFTER DEATH OR SACRIFICE

Type of Graft	Excellent	Good	Excellent or Good	Satisfactory	Poor
Homografts	11(73)	2(13)	13(86)	1(7)	1(7)
Nylon filter fabric	12(48)	10(40)	22(88)	2(8)	1(4)
Braided nylon tubes	5(71)	1(14)	6(85)	0	1(14)
Nylon-polythene-nylon	4(40)	3(30)	7(70)	0	3(30)
Nylon-polythene	5(36)	3(21)	8(57)	3(21)	3(21)
Vinyon-N	5(36)	1(7)	6(43)	2(14)	6(43)

The numerals indicate numbers of grafts; those in parentheses per cent of total.

TABLE III. RESULTS WITH HOMOGRAFTS AND A VARIETY OF PLASTIC GRAFTS FROM STUDY OF ALL ANIMALS\*

Type of Graft	Good or Excellent	Satisfactory	Poor
Homografts	17(90)	1(5)	1(5)
Nylon filter fabric	35(92)	2(6)	1(3)
Braided nylon tubes	14(88)	1(6)	1(6)
Nylon-polythene-nylon	12(80)	0	3(20)
Nylon-polythene	14(70)	3(15)	3(15)
Vinyon-N	8(50)	2(12)	6(38)

\*Animals still alive with good femoral pulses are considered to have a good result.

The numerals indicate numbers of grafts; those in parentheses per cent of total.

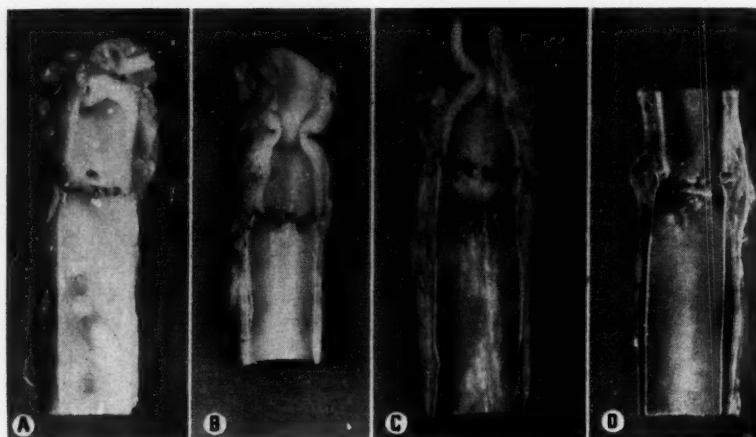


Fig. 3. Photographs of portions of four nylon filter fabric grafts and the adjacent ligated aorta, 180, 120, 60 and 30 days after implantation. (From Harris, E. J., et al: Arch. Surg., 71:449, 1955.

marized, with consideration given only to those grafts examined post mortem. It will be seen that good or excellent results were obtained in from 85 to 88 per cent of the homografts, nylon filter fabric grafts and the braided nylop tubular grafts, while poor and satisfactory results were noted in only a small percentage. The per cent of good and excellent results in the other three types of grafts ranged from 43 to 70. In these groups, the poor results varied from 21 to 43 per cent.

In Table III the outcome in all the animals is analyzed, including those which are surviving. Here grafts in living dogs with strong peripheral pulses are considered as having a good result. Approximately 90 per cent of the homografts, nylon filter fabric grafts and braided nylon tubes had good or excellent results. In roughly 5 per cent of each the outcome was satisfactory and in another 5 per cent, poor. In the other three groups, from 50 to 80 per cent had good or excellent results.

It is apparent that the results with nylon filter fabric grafts were better than those with the two sorts of fused nylon and polythene and with Vinyon-N. If the smaller series observed over a comparatively brief period is significant, the crimped braided nylon tube grafts also are quite satisfactory.

All those who engaged in these studies agreed that the freeze-dried homografts were superior to all the plastic grafts from the standpoint of ease of interpolation and the appearance of the graft up to periods of approximately one year. However, the nylon filter fabric grafts proved altogether quite satisfactory (Fig. 3). They were a bit more difficult to suture to the host aorta but were anastomosed with relative ease and rapidity. About the same percentage gave good or excellent results and the percentage of poor or only satisfactory results was correspondingly low. They became thoroughly incorporated in the new aortas built about them by the host (Fig. 4). The same seems to be true of the braided

nylon tubes. They were easily affixed to the aorta and yielded a high percentage of good and excellent results (Figs. 5 and 6). When successful, the Vinyon-N grafts resulted in quite satisfactory new aortic segments (Fig. 7) but, in

### Clinical Experiences

*Aortic and Aortic Bifurcation Grafts.*—My experience has been limited. Altogether twenty-five plastic grafts have been used to replace seg-

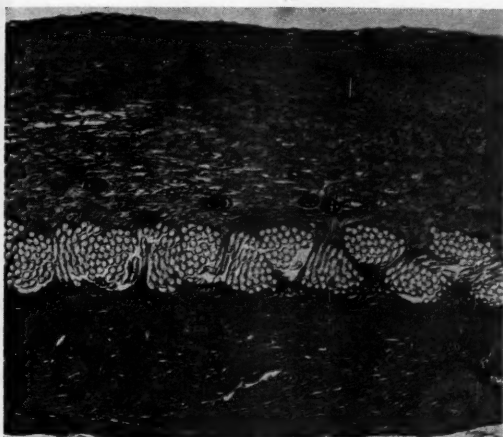


Fig. 4. Photomicrograph of nylon filter fabric graft 120 days old. (From Harris, E. J., et al: Arch. Surg., 71:449, 1955)

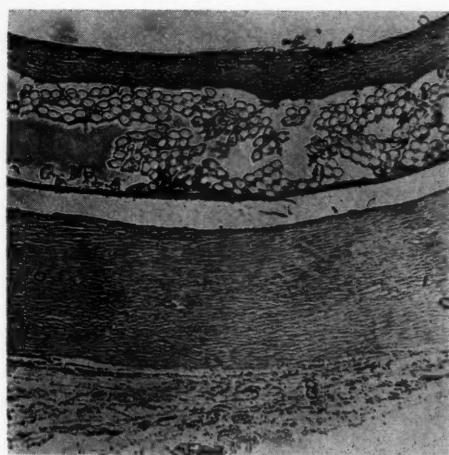


Fig. 6. Photomicrograph of braided nylon graft sixty days old. The defect in the nylon and the separation of layers is an artefact due to sectioning.



Fig. 5. Photograph of portion of chemically treated braided nylon tubular graft and adjacent aorta 112 days after implantation.

our hands, they gave the highest incidence of poor results. The fused nylon and polythene grafts more often yielded good results than those of Vinyon-N but were inferior to grafts of nylon filter cloth and the braided nylon tubes.

ments of the aorta and the aortic bifurcation (Fig. 8). Unfortunately, not all of the patients survived. In all but two of those who died following operation a post-mortem examination was carried out with demonstration of patency of the graft. In one of the exceptional cases, a man of sixty-one with a previous history of myocardial infarction, death in circulatory collapse occurred two days after operation and permission for autopsy was not obtained. The other case will be described in more detail. The surviving patients have been observed over periods ranging from a few weeks to twenty-three months. Their grafts have remained patent. In addition,

## PLASTIC REPLACEMENT OF ARTERIAL SEGMENTS—SHUMACKER

I know of a small number of cases in which other surgeons have used with success grafts of fused nylon and polythene and grafts of the nylon filter cloth.

hospital on June 11. There was moderate drainage at that time. When seen on July 2 he was still having slight drainage but was feeling well and had excellent circulation in his lower extremities. On July 28 he stated that he had begun to drain a small amount of

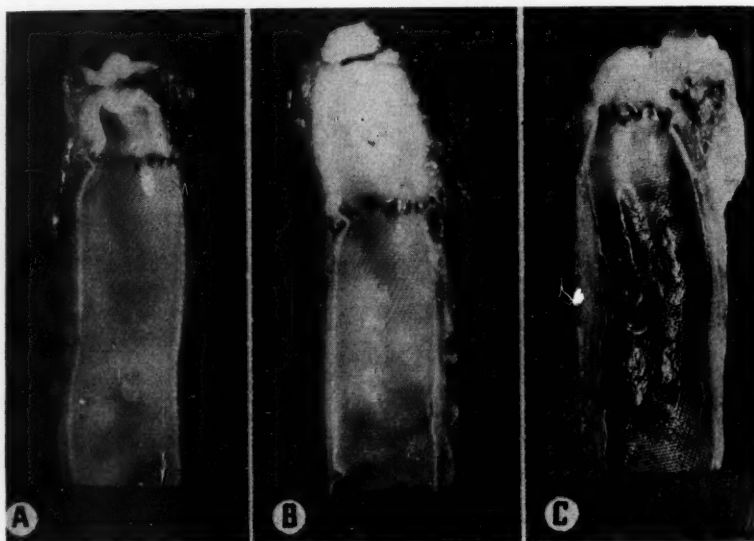


Fig. 7. Photographs of portions of three Vinyon-N grafts and adjacent ligated aorta 180, 120, and 60 days after implantation.

Heat-fused grafts of two layers of thin nylon and a single layer of polythene film were used in fourteen instances. Two were straight aortic grafts, five were anastomosed to the aorta above and the common iliac arteries below, five were interposed between the aorta above and one common iliac and one external iliac artery below, and in two cases the graft was interpolated between the aorta and both external iliac arteries. They all were sutured in place without undue difficulty and they served well as conduits. Difficulty was encountered in one case.

A man, aged sixty-three, who underwent excision of a large abdominal aneurysm on May 14, 1954. It involved the proximal portion of a very badly diseased left common iliac artery and extended down to involve the external iliac and hypogastric arteries on the right. The graft was sutured to the aorta, the left common iliac and the left external iliac artery. His immediate recovery was good and there were excellent pulses in both lower extremities. However, on May 23 he developed fever, and by June 4 it was clear that he had a retroperitoneal abscess. On that date a very large infected hematoma was evacuated and drained through a muscle-splitting extraperitoneal incision. The entire graft lay in the abscess cavity and was completely surrounded by infected material. The fever disappeared promptly and he was discharged from the

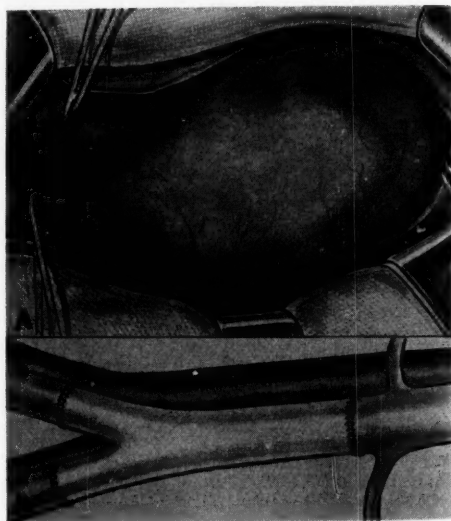


Fig. 8. Drawing of typical abdominal aortic aneurysm and interposed plastic graft after its excision. (From Shumacker, H. B., Jr., and King, H.: *Surg., Gynec. & Obst.*, 99:287, 1954.)

bright bloody fluid from the sinus tract two days before. The pulses in both lower extremities were still excellent. He was urged to re-enter the hospital, but in spite of persistent warning he remained at home until August 19.

He had had repeated massive hemorrhages from the sinus tract and for a few days also from the rectum. He was nearly moribund on admission. The circulation in both lower extremities was very poor. Hemoglobin was 3.3 gm. and erythrocyte count was 1.39 million. He had passed very little urine during the preceding twenty-four hours, and the urine contained albumin and had a low specific gravity. Non-protein nitrogen was 68 mg. per cent. He was not bleeding. Repeated transfusions of blood were administered and his condition improved. Just before the time of his scheduled operation the following morning, however, he began to bleed massively both from the sinus tract and rectum and his condition rapidly deteriorated. He was taken immediately to the operating room.

There was a large, ruptured, poorly organized aneurysm arising in the region of the left iliac artery and compressing the aorta above and the iliac vessels on the right. The open end of the common iliac artery lay in the hematoma. A small rim of iliac artery was attached to the iliac extension of the graft. There was a relatively fresh thrombus in the graft which otherwise was in good condition. A new bifurcation graft was interpolated. The aneurysm had eroded into the rectosigmoid. The opening was closed and a proximal sigmoid colostomy performed. He died in uremia four days later with a non-protein nitrogen of 155 mgm. per cent and potassium of 7.2. It had been possible to keep the serum sodium and chloride levels normal and, until the last day, the potassium level. No autopsy was permitted.

Under the circumstances which characterized this case it seems clear that any graft might have failed. Actually the graft functioned well in an infected field for over two months. At the final exploration it was impossible to tell whether rupture of the iliac artery or disruption of the graft-iliac suture line had occurred. It was clear that an aneurysm had developed with subsequent rupture through the sinus tract and into the rectosigmoid and with compression and secondary thrombosis of the aortic graft.

A methyl methacrylate coated thin nylon graft was used in a single case. It was a long bifurcation graft between the aorta and both common iliac arteries inserted after excision of a large aneurysm. The patient has done well and the graft has functioned nicely for seventeen months.

Nylon filter fabric grafts have been used for aortic replacement in ten cases (Fig. 9). Five were straight aortic grafts and four were bifurcation grafts between the aorta and both common iliac arteries. One was a curved aortic graft replacing a portion of the arch and almost all the descending thoracic aorta. Two of these patients died, both with straight thoracic aortic grafts. Their grafts were found patent on post mortem study. The remainder are well with

nicely functioning grafts from a few weeks to nine months after operation.



Fig. 9. Photographs of bifurcation and straight aortic grafts made of nylon filter cloth and braided chemically treated nylon tube for smaller artery replacement. The nylon filter fabric grafts have been stuffed with cotton before photographing. The crimped braided tube is seen to bend without kinking.

*Smaller Grafts.*—My experience with smaller grafts in patients has been even more limited. Altogether I have used eight such grafts and my associate, Dr. T. C. Moore, two additional grafts. Only in four of these cases was there a patent distal arterial tree. In the others there was distal obstruction and completely inadequate "run-off." In the four favorable cases an excellent result was obtained. All were braided nylon tubes interpolated end-to-end to the artery proximally and distally. One was a common iliac, one a subclavian, and two femoral grafts. Three other braided nylon tubes were used in relatively hopeless cases. Two femoral-popliteal grafts failed. In one case in which it seemed most unlikely that the graft would succeed it worked well. In this patient a long graft was sutured end-to-side to the proximal portion of the thromboendarterectomized common iliac artery and to the common femoral artery. Thromboendarterectomy of the entire femoral and popliteal arteries was carried out, but the terminal portion of the popliteal could not be reopened and blood flow

through only small branches was restored. In one case a nylon-polythene-nylon graft was interpolated between the aorta and femoral artery. There was no retrograde flow of blood and the limb was completely ischemic. The graft did not remain patent. In two similarly unfavorable cases, nylon fabric grafts failed. One was between the aorta and femoral artery, the other between the common iliac and femoral artery. In this small series the grafts were successful in four favorable cases as well as in one in which it was thought the chances of success were very poor. The failures occurred in cases in which it is doubtful that any type of graft would have remained patent.

### Discussion

A number of plastic materials have now been evaluated as arterial substitutes. Vorhees, Blake-more and Jaretzki<sup>5,11</sup> and D'Angelo and his associates<sup>12</sup> have studied Vinyon-N, as has my own group.<sup>8,9</sup> Though some excellent results have been obtained, the use of this material has resulted in a significant percentage of failures. The leaking of blood through the cloth is an additional handicap and pre-clotting of the cloth to obviate this difficulty may have some disadvantages.<sup>13-15</sup> Hufnagel and Rabil have gotten good results with orlon.<sup>13,14</sup> From their analysis of physico-chemical characteristics of a number of plastics, Deterling and Bhonslay<sup>15</sup> concluded that dacron might be the best material, with orlon and nylon as close second choices. Their small experience was good with grafts of these three materials. Shumway and his colleagues<sup>16</sup> from short term observations report excellent results with prostheses made of polyvinyl sponge. From the available literature and our own studies, it appears that at least nylon, orlon and dacron are suitable for plastic vascular prosthetics and undoubtedly other plastics also can be used for this purpose. Our own work leads me to prefer at the present nylon filter fabric grafts for aortic and simple aortic bifurcation replacement and the chemically treated braided nylon tubes of Edwards and Tapp for small artery substitution or by-pass.

Clinical experiences as yet recorded in the literature are small. I know that a number of surgeons have had successful cases which are not yet reported. The anastomosis of homografts is somewhat easier to perform than the union of

any plastic tube with the host artery and yet the latter can be interpolated without any real difficulty. There are certain advantages of the plastic prostheses. They are readily available, easily sterilized, and can be constructed to fit the individual demands of the patient. This point is illustrated by a recent case in which a huge ruptured abdominal aortic aneurysm was excised. The abdominal aorta above and below the aneurysm was markedly dilated. A graft was quickly made to fit the proximal and distal aortic ends. It was 15 cm. in circumference at the upper end, and 12 cm. in circumference at the lower end. No homograft could have fitted so well. The plastic material is relatively indestructible and one would presume it would lend strength to the newly formed artery for an indefinite period of time.

It has proved even more difficult to obtain smaller artery homografts than aortic homografts. For this reason, I have used principally venous autografts and plastic grafts for replacement of arteries other than the aorta. At the moment I prefer grafts made of nylon filter cloth for aortic and simple aortic bifurcation replacement. Only careful follow-up studies of many patients will establish better the relative merits of homografts on the one hand and plastic grafts on the other.

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## PLASTIC REPLACEMENT OF ARTERIAL SEGMENTS—SHUMACKER

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### Discussion

F. JOHN LEWIS, University of Minnesota: It is now clear, through the significant work of Dr. Shumacker and others, that plastic vessels may be used successfully to replace at least some parts of the arterial tree. The artery ultimately obtained is certainly not a normal one but it is usually better than the diseased one it replaces and it is probably as good as the vessel that results from a homograft.

A number of different fabrics have been advocated, and so a study like Dr. Shumacker's which sets out to measure the relative merit of various plastic arteries is an important one. We are engaged in a similar project which has not yet progressed as far. In our study, however, we are investigating not only cloth arteries but also vessels made of a different type of plastic. This plastic is not cloth, but rather a polyvinyl sponge (Ivalon®).

As Dr. Shumacker began his work by repairing experimental, septal defects with nylon, we too started within the heart and used molded plugs of Ivalon to close experimental ventricular septal defects. These devices were well tolerated and we were impressed with the adaptability of the material. It could be permanently molded into almost any shape and density simply by boiling it. Tubes that had the elasticity and consistency of arteries could be made so that they were impervious

to blood but still porous enough to allow fibrous tissue in-growth. They are easy to stitch in place because they hold their form and hold stitches without tearing.

In dogs these Ivalon arteries have worked well in the abdominal and thoracic aorta. In a few animals followed for over one year abdominal grafts are still patent but not dilated. It is relatively easy to make substitutes for the aortic bifurcation with this material and more complicated vessels can be constructed, as well. We have made Ivalon aortic arches and substitutes for the abdominal aorta from the level of the diaphragm down with all the major branches. Pleated vessels similar to the woven nylon tubes of Edwards and Tapp can be made, and we have even tried to make a cusped aortic valve with the material.

Unfortunately, these plastic replacements are never transformed into normal arteries. They become, in time, firm, fibrous tubes instead. The lively elasticity of newly made Ivalon arteries is soon lost, but this is a characteristic of all arterial substitutes. Some plastic arteries may have fewer undesirable characteristics than others, and a number of them may, for various reasons, actually be better than homografts. This is a difficult evaluation to make but it can be accomplished through studies such as the excellent one that Dr. Shumacher has described.

Without the host of willing volunteers who annually comprise the Heart Fund army, the battle against heart disease could never have been joined.

In its earliest years, the Minnesota Heart Fund relied largely upon a small group of physicians for direction of the campaign. Although their time was limited, this group succeeded in establishing a financial "beachhead."

Then, in 1951, members of the Minnesota Association of Life Underwriters volunteered to adopt the Heart Fund as their state-wide service project.

Bringing their innate salesmanship and enthusiasm into the annual February campaign, this group was

instrumental in rapidly accelerating the financial growth of the Heart Fund.

Realizing that the manpower of their organization was not great enough to conduct more intensive drives, the group called upon Minnesota housewives for assistance.

In 1954, a "Heart Sunday" army of these housewives staged a one-afternoon collection of funds for heart research. The result was inspiring. In the span of just four hours, more than \$110,000 was collected. Results in 1955 were even more gratifying, and the 1956 "Heart Sunday" idea will be expanded to cities throughout the state on February 26.



## PRESENT TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

WENDELL H. HALL, M.D.  
Minneapolis, Minnesota

It is ten years since the first patients with subacute bacterial endocarditis were successfully treated with penicillin in large doses. It is worthwhile to survey what we have learned in the past decade about the treatment of this malignant disease. The interested reader may wish to refer to two recent and extensive reviews of the subject.<sup>1,2</sup>

It is obvious that no chemotherapy should be given until several venous blood cultures have been obtained. In every patient with a positive culture, antibiotic susceptibility tests should be performed. The disc-plate method is not sufficiently accurate for this purpose. Lacking exact susceptibility data, the physician is deprived of the best guide to successful therapy.

Presently, penicillin seldom is given alone. Aqueous penicillin G is generally preferred, usually given intramuscularly at short intervals or by slow intravenous drip. The minimum daily dose is not less than 2,000,000 units and, with resistant infections, may reach 10 to 80 million units. The duration of effective therapy should be not less than six to eight weeks. With very susceptible strains of *Streptococcus viridans*, procaine penicillin 1,000,000 units plus dihydrostreptomycin 1 gram intramuscularly twice daily for two weeks has been successful, but it is not recommended as a routine method.<sup>3</sup> Anticoagulant drugs are dangerous and unnecessary.

All patients with negative blood cultures must

be treated as though the infective organisms were not very susceptible to the antibiotics. With all resistant infections, streptomycin 1 gm. intramuscularly twice daily should be added. Some infections failing to respond to this treatment have been cured with oxytetracycline (Terramycin), or streptomycin plus erythromycin.

Early diagnosis and adequate therapy are important. Unfortunately, death may occur from congestive heart failure, major arterial occlusion or renal insufficiency though the infection be controlled. This is particularly true if the aortic valve is infected. The treatment is costly and uncomfortable to the patient and often difficult for the physician, but with energetic therapy 75 per cent of patients may be spared from an otherwise certain death. Because of valvular damage, those patients who recover may require continued cardiac therapy. Prophylaxis with penicillin should be given during each subsequent serious respiratory infection, and dental or surgical procedure for recurrences are not rare.

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From the Veterans Administration Hospital, Minneapolis, Minnesota, and the Department of Medicine, The Medical School, University of Minnesota.

# Laboratory Aids

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The Minnesota Society  
of Clinical Pathologists  
George G. Stilwell, Editor

## PATHOLOGY HAS EMERGED FROM THE "DEADHOUSE"

GEORGE G. STILWELL, M.D.  
Rochester, Minnesota

A surprisingly large number of people, including perhaps too many physicians, still view the pathologist and his medical specialty in a light that is based on concepts founded so far in the past that their moldiness shows. It is true that pathology during the latter half of the nineteenth century, the pathology of Virchow, was somewhat static "deadhouse" pathology. However, it must be remembered that Virchow died in 1902; many changes have occurred in medical practice during the five decades that have transpired since the death of the "father of pathology."

Far from the least of these changes have been those which have taken place in laboratory medicine. A clear reflection of such changes is seen in the altered professional and economic status of the pathologist. Naturally, the economic returns from any specialty are of little basic importance in the "rating" of the various specialties but they do give some insight into the acceptance of any particular field. The story is told of the physician who went to a medical meeting one wintry day some years ago. Approaching the place of the gathering, he noted a line of Cadillacs. "I see the surgeons are here," he said. Seeing next some Buicks, he stated, "The internists are also here." A line of Fords caused him to say, "Well, the peditatricsians came, too." He entered the building and noted a group of well-worn and wet overshoes. "Ah!" he exclaimed, "and here are the pathologists."

It was just thirty-five years ago that the *Journal of the American Medical Association* carried advertisements for those seeking pathologists under the heading of "Lab. Technician Wanted." The promised returns were commensurate with the obvious scientific rating of the specialty at

that time. The same journal, in its issue dated October 29, 1955, carried an advertisement for a pathologist to direct the department of pathology in a hospital of medium size; the advertisement stated that the guaranteed income and percentage should net to \$35,000.

Times really have changed, both professionally and economically, for the pathologist. No longer is he considered to be somewhat of a medical recluse who chose to fossilize himself with formaldehyde because he did not have the capabilities to become a surgeon or an internist. The modern clinical pathologist probably is expected to know more about the multitudinous fields of medicine both diagnostically and therapeutically than is any other specialist. Recent developments in medicine have drawn him intimately into contact with both the scientific practice and the administration of such fields as clinical chemistry, blood banking, radioactive isotopes, hematology and forensic medicine, to mention only a few. The pathologist certainly is a leader in many of the facets of postgraduate medical education, as witnessed by the fact that in hospital after hospital he is in charge of the teaching program for interns and residents and is responsible for the major part of the clinicopathologic conferences and the general staff meetings.

The extent of the ramifications of medicine with which the clinical pathologist is expected to be familiar is emphasized by perusal of the titles of the original articles listed in the index of the most recent complete volume of the *American Journal of Clinical Pathology*. A brief glance reveals such topics as basic research on new subdivisions of blood groups, heparin, components of thromboplastin, paper chromatography, techniques for determination of protein-bound iodine, spectrophotometric analyses, chemical determinations of such blood constituents as calcium, potassium, chloride, phosphatase, sulfate and

From the Section of Publications, Mayo Clinic.

This is the thirty-fourth in a series of editorial reports sponsored by the Minnesota Society of Clinical Pathologists and designed to foster closer relationships between clinicians and pathologists.

## PATHOLOGY HAS EMERGED FROM THE "DEADHOUSE"—STILWELL

urea, bacteriologic techniques, new factors in the coagulation of blood, radioactive cobalt, cortisone, emission spectrography, Coombs' antiglobulin test, sensitivity tests for antibiotics, microhematocrit methods and various turbidity techniques for hepatic function. Many of these items were unknown fifteen or twenty years ago.

The small list of topics just given might lead one to believe that the modern pathologist has foregone the pleasure of microscopic study of the variegated blues and reds of tissue stained with hematoxylin and eosin. Such is not the case, however. The same journal also contains a wealth of articles devoted to pathologic anatomic diagnosis. Included are discussions of bone-marrow studies, cytologic examination for malignant cells in various bodily fluids, histoplasmosis, hepatitis, mumps, encephalitis, various tumors, rheumatic heart disease, nephrocalcinosis, tuberculosis and gastric granulomas.

These admittedly partial lists of the present interests of pathologists certainly indicate that the modern laboratory physician has removed himself far from the confines of the deadhouse. He plays an important role in modern diagnosis and treatment, both surgical and nonsurgical. Contrary to the older beliefs still held by some clinicians, the pathologist is deeply interested in the "living" patient. Without the services of a good pathologist and the availability of adequate laboratory facilities, it becomes increasingly difficult for the clinician to take full advantage of new diagnostic techniques.

It must be remembered constantly that the pathologist is a consultant in medical practice. He is, of course, familiar with the various techniques employed in his laboratory but the factor of ultimate importance is his broad knowledge of the application and limitation of these methods and the interpretation of their results. The path-

ologist must be familiar with the clinical aspects of many diseases and with their treatment. He is available as a consultant to aid in the choice of the diagnostic procedures that will give the greatest aid to the welfare of the patient at the lowest cost. His interpretation of surgically removed tissues and biopsy material guides the surgeon in the latter's decisions regarding treatment.

Yet, in some localities, the practice of pathology is not considered to be the practice of medicine. As many readers know, a suit has been brought by the hospitals of Iowa against the Iowa pathologists and the attorney general of that state as a result of the official ruling made by the attorney general that the practice of pathology was the practice of medicine.

Obviously, it does not take the ruling of an attorney general to bring out the fact that the pathologist is a practitioner of medicine. Yes, it is true that the modern pathologist still is slightly redolent of formaldehyde from his surgical and necropsy tissues. At the same time he carries a smudge of iodine from the patient whose sternal bone marrow he aspirated an hour ago, a dab of bromophenol blue from a recent test involving paper chromatography, a bit of frost from the blast of carbon dioxide used in a just-completed frozen section of tissue, and a safety badge to guard against an overdose of radioactivity.

Pathologists always have insisted, and justly so, that the practice of clinical pathology is the practice of medicine. They will welcome the internist or surgeon who seeks them out in medical consultation. Their wide experience in so many fields of modern medicine may provide just the hints needed to help solve bothersome problems, thus bringing the greatest possible good to the greatest number of patients.

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## THE MUSHROOM AS A PROTECTIVE AGENT

In Central Europe and in Pennsylvania, folklore credits the eating of certain species of mushrooms with protective effect against development of human cancers. Extracts from ten of eighty species examined do indeed demonstrate some inhibitory effect upon transplanted cancers in mice, report Dr. E. H. Lucas and Joseph Stevens, Michigan State College. The extracts appar-

ently contain some cancer-retarding factor, according to the studies done in collaboration with the Sloan-Kettering Institute, New York. The factor is apparently heat resistant. None of the extracts has yet been purified sufficiently for human experiments, and any role in providing clues toward cancer control is yet unknown.—Medigrams: GP 12:240 B (Oct.) 1955.

# Editorials

JOHN F. BRIGGS, M.D.  
ARTHUR H. WELLS, M.D.  
HENRY G. MOEHRING, M.D.

## COMMUNICATION: AN OVERVIEW

It took World War I, with its recognition of the strategic importance of the communication front, to make us properly aware of the full significance of communication. A more efficient use of language was then imperative. Up to that time, the emphasis, both in high school and college, was on written composition. As the spotlight turned to the broader concept, we began to see that writing was only a small fraction of the process—that reading, speaking, and listening also belonged in the picture.

Early research done by Rankin, at Ohio State University, added to our realization of the importance of this concept. His survey revealed that the average individual spends 70 per cent of his waking time in verbal communication. Of that time, 45 per cent is spent in listening, 30 per cent in speaking, 16 per cent in reading, and 9 per cent in writing.

We also began to be aware of the vital distinction between expression and communication. "Eschew polysyllabic verbal symbols" is expression, but is it communication? "Don't use big words" is more likely to be both.

Gradually, the whole process of communication assumed a clearer perspective. For every writer, we began to think of a reader; for every speaker, a listener. Communication, a sharing experience, demanded a sharing of responsibility if it were to succeed.

A nutrition consultant surveyed 100 pregnant women on their understanding of twenty words typically used in consultation. Although all were natives of Florida, only forty-six knew what was meant by citrus fruit. How often does communication break down partially or completely through failure to understand the capacity of listener or reader?

Furthermore, those of us who are professionally trained have a particular problem. It is easy for the college graduate to forget that college graduates make up less than 6 per cent of our population. Yet, in a democracy, the college-trained 6 per cent must communicate effectively

with the other 94 per cent or distrust and suspicion enter to weaken the unity of our nation. Such terms as *intellectual snobs*, *brain trusters*, or *eggheads* suggest the presence of barriers which must be broken down through increased understanding of the communication process. Efficient communication is the very heart of the democratic process.

Within the last decade, research has begun to come to our help. It has brought new methods of teaching reading efficiency to adults faced with the problem of keeping up professionally in a print-filled world. It is providing needed help in improving listening efficiency for better human relations as well as better learning. Even writing and speaking as they relate to professional status, are being re-examined in an attempt to affect the entire 70 per cent of our communication time. The result should be of benefit to the individual and community as well as to the nation and the world at large.

JAMES I. BROWN  
Professor of Rhetoric

## TUBERCULOSIS CONTROL IN THE SCHOOLS OF MINNESOTA

The Committee on Tuberculosis of the American School Health Association is composed of twelve physicians located in eight states across the nation. The main project of this committee consists of certifying schools with reference to tuberculosis control work in progress. The qualifications for certification consist of testing with tuberculin at least 95 per cent of the children and 100 per cent of the personnel members, including teachers, bus drivers, cooks, and others. All adult reactors, including high school students and personnel members, must have x-ray film inspection of the chest, and those who present shadows which might be due to tuberculosis are completely examined. Those found to have active disease are promptly placed under management.

When children are found to react to tuberculin, an attempt is made to find responsible adult associates as soon as possible.

First in a series of editorials on various forms of communication.

## EDITORIALS

This committee chose Minnesota as the demonstration state to determine the feasibility and effectiveness of such a program. A Minnesota sub-committee consisting of three physicians was appointed, and this committee, working in close co-operation with the state tuberculosis and health association, began work in the early 1940's. The schools of Northfield were the first to qualify and were officially certified in 1945. To date, more than 2300 certificates have been issued to Minnesota schools, and a large number in various parts of the state are about to qualify. It now appears that within the next two or three years every school in Minnesota will have a certificate displayed on its walls. These certificates are signed by the president and executive secretary of the American School Health Association, the chairman of the Minnesota state sub-committee, and the executive secretary of the state tuberculosis and health association.

In Minnesota, there have been numerous instances of teachers, bus drivers and other members of personnel, as well as high-school students, developing contagious tuberculosis without their knowledge and disseminating tubercle bacilli to large numbers of children and personnel members. The certification of schools program spells the doom of such occurrences.

Not infrequently, when this project is started in the school, so much interest has been manifested that it has extended to persons of all ages in entire communities. Usually, local physicians have participated in administering tuberculin tests, making x-ray film inspections of the reactors, and completing examinations when indicated. After the project is completed, many persons later report to their private physicians for periodic tuberculin tests, if previously negative, and periodic x-ray film inspection of the chest, if positive.

This project has been so effective that it has spread to other states. It is now in operation in both Dakotas, Iowa, Illinois, Missouri, and Wyoming. Plans are being made for its adoption in a number of other states.

Here is an opportunity for physicians everywhere to participate in a program that will not only hasten the eradication of tuberculosis in their communities, but also will increase public confidence in them.

J. ARTHUR MYERS, M.D.

## THE FAMILY AGENCY AND MARITAL COUNSELLING

Marital counselling has been one of the primary functions of the private family agency since the beginning of family casework. We prefer, however, not to use the word "counselling," because it implies that the social worker gives advice. We know that telling a couple what to do when the interaction between the two has reached a high emotional state rarely relieves the situation. Therefore, we have developed techniques of working with people so that they learn to understand themselves better in relationship to their marital partners and to their children. We use the term "family casework," because conflict between a husband and wife has its effect on the children. Sometimes a marital relationship goes along quite well until children are born and the responsibilities placed on both partners becomes greater. This added responsibility, with certain combinations of personalities, throws the interaction between husband and wife out of balance, and in extreme cases the wife may even have a postpartum psychosis.

In our work with families, we think in terms of the "alcoholic marriage." Case examples show that certain types of women tend to marry the men who drink to the extent that they may be classified as "alcoholics." The woman's personality is such that while she is concerned about her husband's excessive drinking which deprives the family of material things, she at the same time handles her husband in such a way that his drinking becomes worse. She seems to have an unconscious need to have an alcoholic husband.

We diagnose our family situations in terms of typical axes, around which family relationships revolve. The Community Research Associates, Inc., sponsored a pilot study in Saint Paul, Minnesota, using Family Service case records. The study took place in 1952 and is the beginning of a classification framework for family-oriented social diagnosis. The second phase of the Classification Project is going on at the present time. Seven family agencies, including Family Service of Saint Paul, are taking part in this research project.

We have learned from our large body of knowledge that certain types of men tend to marry certain types of women, and vice versa. With

Fourth in a series of editorials on Family Service.

few exceptions, most marriages go along quite well until some crisis arises. With case-work help, many marriage relationships can be put back in balance. Some marriage relationships, when diagnosed, show that in reality the relationship was never a "marriage." When a marriage does end in divorce, each partner needs help in seeing what his part in the relationship was. Each man and woman tends to seek in the second marriage the same kind of personality that he sought in the first marriage. This is why we often see the same man or woman entering into more than one marriage, and with the relationship ending each time in divorce.

To date, we have tentatively formulated ten relationships. They are:

1. A dual immature dependency axis.
2. A woman-oriented anxiety axis.
3. A woman-dominated dependency axis.
4. A woman-dominated competitive axis.
5. A man-dominated competitive axis.
6. A man-oriented, self-depreciating axis.
7. A woman-oriented, self-depreciating axis.
8. A dual emotionally detached axis.
9. A man-dominated hostile axis.
10. A woman-dominated hostile axis.

These ten relationships were formulated from studying 100 families. We are assuming that there are more, and continued research is being carried out to determine whether other classifications of emotional axes and personality types may be found among families with problems. These ten descriptions are not inclusive in themselves. They are descriptive headings we are using to distinguish the relationships. The classification is made after detailed study of the personalities that make up the axis.

Case-work has developed methods of treatment in dealing with people who are having difficulty in their relationships. Their methods vary from the manipulation of the environment when the crisis that upset the marriage is primarily an environmental factor to the method of "clarification" which helps the man and woman have better understanding of themselves in relationship to each other. Each family situation may need not only one but a combination of two or more treatment methods in dealing with the problems of marriage.

(MRS.) LOIS HOFFMAN  
*Director of Case Work Services*

## SUBURBAN MEDICAL MIGRATION

Ever since man began practicing medicine, people have been "going to the doctor." But times have changed. Today, doctors are "going to the people."

With America's population steadily increasing, practically every major city is experiencing residential expansion. And much of this expansion is taking place in the suburban areas, as new families overflow city boundaries. As a result, physicians are locating where the people live—with offices in outlying business districts, and in more recent years, in or near major shopping centers.

An informal study of the location of physicians' offices in the city of Saint Paul, for example, shows that there are actually more general practitioners located in outlying areas than in the downtown "loop" area. A total of 171 have outlying offices, while 140 maintain downtown offices.

Specialists, however, still seem to prefer downtown. In Saint Paul, almost all of them—139 to be exact—have downtown offices. The few specialists who have offices in the outlying areas are principally pediatricians or obstetricians.

Outside of the fact that many hospitals—especially the newer ones—are located in residential areas, there are other reasons why physicians are locating in or near the major shopping centers. Convenience for the patient is probably most important. The young mother with three or four small children certainly finds it easier to get to her physician's office if it is located at or near where she does most of her shopping. She doesn't have to "dress up" as she does when going downtown. If she doesn't have the family car during the day, she can quite often walk to her physician's office. If she does have to use public transportation, the ride is usually quite short. And, certainly, an outlying office offers many conveniences for the elderly patient.

Another factor to consider is that many shopping centers now have nurseries where the mother can leave her children while she shops. This same nursery could be utilized by the mother when she visits the physician.

Another reason shopping centers are attracting physicians is that shopping centers of the future will be more than groups of stores. They are developing into civic and cultural centers

## EDITORIALS

with additional facilities for entertainment, recreation and other activities.

Although the physician is not primarily concerned with the "business prospects" of a shopping center, it should be noted that many of the smaller centers are doomed to failure, because for want of careful planning they are so close to each other that they are in competition. So in contemplating the location of an office in a shopping center, careful attention should be paid as to whether or not the shopping center will attract the large numbers of people it is supposed to serve.

It is also entirely possible that the physician locating his office in or near a shopping center will be placing even more stress on evening hours, to conform with the shopping habits of the people living in the area. Many large centers are open three nights a week, others as many as five nights. The reason for this is that shopping is becoming more of a family affair, and evening is about the only time Dad is free. Thus, evening hours might be more convenient for more people.

Another possible future development is that shopping center planners will be including a "Medical Center" as part of their group of buildings, with street-level entrances. At the present time, physicians are using mostly second-floor locations.

If our present population trend continues—and there seems to be every reason that it will—both the new physician and the established practitioner would do well to investigate the many advantages they could offer their patients by locating in the outlying areas.

If the developers and investors in the outlying areas do not provide suitable office facilities, then, of course, it becomes necessary for the physician to consider the construction of his own facilities.

Because, more and more, the doctors are "going to the people."

A. E. REHNBERG  
*Saint Paul Realtor*

### A TREND OR MORE?

What assembled criteria would constitute a trend, we don't know. We also don't know the noun of assembly (you remember the *herd* of sheep, the *pride* of lions, the *gaggle* of geese—and the *carton* of Camels) that would be applied to such criteria. However, when a series of related events come on us in a short space of

time, we think more than coincidence is at work. For example, we can't explain, with or without statistics, these conjunctions except as at least a trend:

First, we ran into a statistical summary demonstrating an increased incidence of injuries from home tools, over weekends—to folks who were doing-it-themselves.

Second, we received a letter from a colleague who gave us advice about which tools and techniques to use in refurbishing a basement wall. His final advice was, "... and get a good supply of Band-Aids."

Third, we took judicial note of a look-out-for-the-do-it-yourself-accidents in a *New England Journal of Medicine* editorial.

Fourth, ditto for a do-it-yourself cartoon with a *get-well-quick* card display prominent in the foreground.

And last, another colleague showed us the almost healed amputation stump of his left thumb, the result of the ministrations of a power saw and a surgeon, in that order.

Now, what with the winter season well upon us and less chance for venting excess energy out of doors, and with the natural urge to do this or that around the house while weather-bound, or to make this or that present in some spare time, we are impelled to lay these matters before you, and suggest that some folks have spent their technical careers acquiring skills, the exercise of which you are now trying to deny them by doing-it-yourself.

Anybody know where we could get a 1/4-inch power drill complete with 1,001 attachments? Cheap?

—H.G.M.

### FIFTH PRINTING OF DIABETES PAMPHLET

In January, a reprint of "Diabetes: How to Make It Harmless" will be issued by the Committee on Diabetes of the Minnesota State Medical Association, under the chairmanship of John R. Meade, M.D., Saint Paul. There will be revisions to bring the pamphlet completely up to date.

This pamphlet teaches all that is necessary for a patient to know to enable him to manage his condition safely. Any diabetic may have a copy if he first obtains the approval of his physician. Besides general instructions of value, there are many sample menus.

This is the fifth printing of the pamphlet. It was first published in 1934 by the Committee on Diabetes, MSMA, while Russell M. Wilder, M.D., Rochester, was chairman.

# President's Letter

## NO TIME FOR LITTLENESS

With the approach of the Christmas season and its age-old theme of "Peace on Earth, Good Will Toward Men," it is well that we gain new faith and encouragement in the furtherance of the tenets of our profession. Why? Because the message of the Christmas season allows no place for petty bickering, selfishness, personal jealousy, nor minority pressure groups. Our profession and the medical organizations are dedicated to the furtherance of the health of the people of our community, and anything that interferes with this objective is directly contrary to the spirit of Christmas. Good will toward all men is a challenge as well as a responsibility of our professional organization.

It has never ceased to be a source of amazement to me that small groups of our fellow citizens will seek to impose doctrines and procedures upon their fellow men by any means whatsoever, even though history, experience, common sense and professional expert knowledge all point to the fact that they are against the public interest. Is it because of ignorance, willful or otherwise? Is it because of a thirst for power, or personal aggrandizement? Is it for financial gain, or is it because, in some distorted minds, certain persons feel superior to their fellows and seek to impose their will and regulatory way of life upon them? The answer probably is a combination of all of these reasons. They are little men, small in spiritual stature. They have deviated far from the teachings of the Great Master, whose birthday we shall soon celebrate.

December also brings to a close my year as president of the Minnesota State Medical Association. It is with a sense of inadequate accomplishment and frustration that I leave this office, to which you elected me eighteen months ago.

I am grateful for the honor which you have given me, and assure you that it has been a privilege to work with the other officers, council, and executive officers of our association. They have all been most helpful, and especially is it true of the State Association office staff. To my own professional associates and staff, I am especially grateful for their understanding and aid in furthering the work of our organization.

I am sure that each president hopes that he has left some small imprint of his personality and ability upon the state organization. In the past, we have never suffered from lack of leadership, and I am sure that the future will enable dedicated men to serve the association and our profession with the same zeal that has been exhibited by my predecessors.

The work of our organization is never-ending. The "little men" and the minority pressure groups are forever seeking to hamper the work and the accomplishment of the objectives to which our association is dedicated. Eternal vigilance is the price of not only liberty but of progress, in attaining the ends toward which we all strive. The endless battle should not be a source of discouragement, but rather a challenge for us never to compromise with principle, never to succumb to the "little man's" level of personal or professional selfishness. In other words, inculcate forever into our work the Christmas spirit of "Good Will Toward Men."

It is my personal wish that each of you and your loved ones have a blessed Christmas season.

*Arnold O. Swenson*

President, Minnesota State Medical Association

# Medical Economics

Edited by the  
Committee on Medical Economics,  
Minnesota State Medical Association  
George Earl, M.D., Chairman

## COUNTY SOCIETY STUDIES DOCTORS' ESTATES

Revealing facts are seen in a recent small, but meaningful survey of obituaries of physicians, made by the Hartford County (Connecticut) Medical Society.

The survey showed that one out of eight of the physicians who died between 1940 and 1953 was in debt at the time of death. The survey is reported by a recent AMA Secretary's Letter, noting that the number of deaths studied was 144.

Also, of the estates studied, one out of three left net assets of less than \$10,000.

According to the report, "The Hartford survey disclosed only one extremely wealthy doctor out of the 144 and that \$575,915 of his estate was consumed by estate taxes and other settlement expenses. Only one doctor in eight survived his wife."

### Death Rate High

The report also showed that deaths among doctors aged forty to fifty occurred in a ratio of 2:1 compared with the general population, and in the sixty to seventy age bracket, the doctors' death rate was 50 per cent higher than that given for the same ages in the insurance table. As would be expected, heart disease and cerebral hemorrhage were the chief causes of death.

The age of death of the physicians, when compared with life insurance mortality tables, showed that there were two vulnerable age periods for medical men—forty to fifty and sixty to seventy.

## MEDICAL COSTS SURVEY NOTES TRENDS

Only 26 per cent of the adult population believe that the cost of medical care in America is much too high. This figure is reported in a recent survey of opinions and attitudes toward medical care just released to the pharmaceutical industry by the Health Information Foundation of New York. Other results show that 40 per cent of the adult population believe food costs are much too high; 45 per cent believe repair charges (TV,

auto, et cetera) are excessive; 27 per cent are equally critical of clothing costs.

The survey notes:

"While medical costs in general come in for less criticism than other elements of the cost of living, within the category of medical costs, the percentage believing costs 'much too high' for doctors' fees is 16 per cent; hospital charges, 39 per cent; dentists' fees, 24 per cent; prescriptions at drug stores, 38 per cent."

Another interesting fact is that 56 per cent of the population cannot give the name of one company that, they believe, manufactures a new or "wonder drug."

When asked the question, "What are some of the things that make it easier to have good health today than it was thirty years ago?", 71 per cent cited improvements in medical knowledge and facilities, and almost half the population (47 per cent) specifically referred to new drugs, medicines, and vaccines now available.

### Prescription Costs

Further information shows that 38 per cent of the population believe that cost of prescriptions is much too high, and 28 per cent believe that costs are somewhat higher than they should be. The report states:

"Of those giving reasons for high cost in this category, less than half attach blame to anyone. Twenty-six per cent of those who complain of prescription costs blame the druggists, 10 per cent mention physicians and 7 per cent pharmaceutical manufacturers. An additional 16 per cent blame some unspecified 'they.' Some individuals mention more than one person or group."

This question was also asked: "What people or groups do you think have been mainly responsible for these new 'wonder' drugs?" The answer:

"... only 11 per cent of the respondents give specific credit to the drug companies, pharmaceutical houses, the chemical industry, or drug manufacturers; an additional 9 per cent mention 'laboratories'; 23 per cent credit doctors, the American Medical Association, or groups of doctors; 40 per cent credit scientists, science, research, or persons such as medical researchers and chemists."

## GRADUATE MEDICAL EDUCATION SHOWS BIG GAINS

According to a recent news release from the Council on Medical Education and Hospitals of the AMA, "training programs for newly-graduated doctors have become as big—in terms of enrollment and time spent—as basic medical school education." It is believed that this situation is unique among the professions, the news release stated.

The release notes that enrollment of young physician graduates as interns and residents for the 1954-55 year passed that of students in undergraduate medical schools. It also notes that this is an indication of "the magnitude of the growth of graduate training over the past ten years."

### Figures Tabulated

The Council's annual report on internships and residencies showed 9,066 graduates serving internships for 1954-55 and 20,494 serving as residents, a total of 29,560 in 1,364 hospitals. This is an increase of about 2,500 over last year. Internships offered show for 1954-55 a 250 per cent increase over the number reported in 1914, the first year approved hospitals were listed by the council.

### Trend Reversed

The Council reports that "this year's internship and residency figures reverse the trend of the past several years, when unfilled positions were increasing." The report showed foreign medical school graduates in 1954-55 filling almost half of the vacancies not taken by American graduates, thus alleviating partly the demand for hospital staff appointees.

### Residency Training

Another important change reported by the Council was in requirements for residency training, which follows internship as the next step after medical school graduation. The Council reported that previously some programs offered specialist certification training which almost could be compared to allowing a medical student to receive his M.D. degree after "completing four successive years at the freshman level at four different medical schools." The new policy eliminates the possibility of taking specialty training in several separate programs and instead requires stricter continuity in an integrated training course.

## Cash Stipend Higher

The Council's report stated that the average cash stipend paid to interns by hospitals affiliated with medical schools was \$87 a month compared to \$84 a month last year. Hospitals not affiliated with schools pay \$136 a month on the average, an increase of \$1 over last year. The report also said that figures indicate that the amount of stipend, as usual, has no effect on the prospective intern's choice of a hospital for training.

"Federal hospitals, such as armed services of VA institutions, and local governmental hospitals," the report concluded, "offer 36.5 per cent of all available intern positions and have the highest rate of filled positions. Their rates range from 100 per cent for the Public Health Service, 99 per cent for Army hospitals, and 97 per cent for Navy. County and city-county hospitals have rates of between 93 and 96 per cent."

## SUGGESTIONS ON JOINT COMMISSION ON ACCREDITATION WANTED

At the American Medical Association convention last June, a committee was appointed to study the functions of the Joint Commission on Accreditation of Hospitals. The committee is now asking physicians for any observations or suggestions concerning the work of the Joint Commission.

The committee is interested especially in the following:

1. The general understanding by physicians of the functions of the Joint Commission.
2. Whether the method of appeal from an adverse ruling regarding accreditation is satisfactory.
3. The effect on the individual physician's hospital connections due to actions of the Joint Commission.
4. Whether any organizations not now represented should have official representation on the Joint Commission.
5. The effect of the Joint Commission's requirements concerning such matters as staff meetings.
6. The pros and cons of separating administrative and professional accreditation functions in the inspection of hospitals.
7. Constructive suggestions for improving the hospital accreditation program.

Any comments from individual members or state and county medical societies should be ad-

dressed to: W. C. Stover, M.D., Chairman, Committee to Review Functions of Joint Commission on Accreditation of Hospitals, 535 North Dearborn Street, Chicago 10, Illinois.

Committee members will report on their findings at the next American Medical Association meeting. It is important to co-operate in this effort if the Joint Commission is to function usefully.

### **SOCIAL SECURITY, OASI FIGURES NOTED**

Latest information from the Social Security Administration is reported in a recent AMA Washington Letter, and reveals that the proportion of people receiving old-age assistance payments (based on need) has declined 20 per cent in the last five years, but because states are increasing the amount of individual payments, the total expenditure has increased. "At the same time," the report says, "figures released by the agency indicate that in the same period the proportion of old people receiving old age and survivors payments has increased by about 150 per cent."

The report quotes the administration's comment on the drop in numbers receiving old-age assistance:

"The economic prosperity of the nation is reflected to some extent in this decline. Another major reason is the continued growth in the number of aged persons who now receive benefits under the old-age and survivors insurance program."

Further explanation is:

"The 150 per cent increase in proportion of OASI recipients is explained only in small part by shift of elderly assistance cases to the pension rolls; most of the increase was caused by congressional action in extending coverage to additional occupations and making it increasingly easy for older persons to qualify for pensions."

### **Population Noted**

The report says that in June, 1950, the aged population (sixty-five and over) numbered 12,399,000, of whom 2,786,690 (225 of every 1,000) were receiving old-age assistance. Latest data (June, 1955) show in the sixty-five-and-over age group a population of 14,244,500, of whom 2,544,496 (179 in every 1,000) were receiving old-age assistance.

In June, 1950, approximately 169 in every 1,000 aged persons (about 2,094,000) were receiving OASI pensions. Five years later, 423 in every

1,000 (6,025,000) were receiving OASI pensions, a proportional increase of about 150 per cent. The month of June is used by the Social Security Administration to demonstrate what has been happening to the old-age assistance program. Five years ago, payments for that month totaled \$122,350,000 (an average of \$43.85 to the 2,790,000 recipients). Last June, the rolls had dropped to 2,549,000, but total payments had increased to \$133,297,000 (an average of \$52.30 per recipient).

### **New York Medicine Says:**

"It would cost an extra \$2,000,000,000 per year for the next twenty years to implement H.R. 7225 and then \$2,500,000,000 a year thereafter. To finance the gigantic increase, Social Security taxes over twenty years would increase from the present 2 per cent to 9 per cent . . . a jump of four and one half times.

"In deciding to fight H.R. 7225 the Board of Trustees of the AMA have made a major change of policy. The AMA, it may be recalled, has never fought the Social Security laws as such but on the point that physicians should not be included in Social Security coverage of the self-employed. Now it will attack a proposed section of the law which applies . . . not to physicians alone but . . . to the rest of the population."

### **FOLSOM ASKS MORE FUNDS FOR MEDICAL RESEARCH**

Secretary Folsom, HEW, favors more funds for medical research in crippling and fatal diseases. His address of welcome at the third annual Symposium on Antibiotics is reported in a recent Washington Letter of the AMA.

Mr. Folsom noted that Congress approved this year more than \$97 million to investigate causes and treatment of major illnesses, or about twelve times the amount spent in 1946.

He stated: "In addition to these government expenditures, the pharmaceutical industry and many other private groups spend many millions of dollars for research yearly. We must seriously consider making even more funds available for medical research to bring even greater benefits to humanity."

Mr. Folsom described progress in antibiotic therapy during the past thirteen years as phenomenal. The antibiotic industry, non-existent in 1942, now has a capital worth of over \$1 billion; antibiotics, once produced in milligram quantities, are now measured in tons, and untold numbers of people are alive today because of the drugs, he said.

# The Dean's Page

## MINNESOTA GRADUATES IN PUBLIC HEALTH WORK

I have just returned from the Eighty-fifth Annual Meeting of the American Public Health Association in Kansas City, and I want to share with the physicians of Minnesota my great sense of pride and satisfaction in the prominent and distinguished part that Minnesotans played in this meeting.

In the first place, the President of the Association, who presided at the meeting, was Dr. Herman E. Hilleboe, M.D., University of Minnesota, 1931, Health Commissioner of New York State. The President for next year is Dr. Ira Hiscock of Yale, and chosen as the new President-elect for 1957 is Dr. John W. Knutson, D.D.S., University of Minnesota, 1931. Incidentally, Doctor Knutson becomes the fifth out of seven consecutive presidents of the American Public Health Association whom we can claim as a Minnesotan. The first was Dr. William P. Shepard, M.D., University of Minnesota, 1922, and M.A. in 1924, President of the American Public Health Association in 1951 and currently Second Vice President of the Metropolitan Life Insurance Company; the second, was Dr. Gaylord W. Anderson, Director of our University of Minnesota School of Public Health, President of the American Public Health Association in 1952; the third was Dr. W. L. Halverson, born and raised in Litchfield, Minnesota, Commissioner of Health of California, and American Public Health Association President in 1953; the fourth was the current President, Dr. Herman E. Hilleboe; and the fifth, the new President-elect, Dr. John W. Knutson.

Several of the most distinguished awards in medicine and public health were conferred upon Minnesotans at Kansas City: Dr. Albert J. Chesley, whose name is synonymous with public health in Minnesota, was given posthumously the Sedgwick Medal for "distinguished service in public health." This was accepted by Dr. Robert N. Barr, Doctor Chesley's successor as Executive Secretary of the Minnesota State Board of Health.

Another award conferred upon Minnesotans at this meeting was the Albert Lasker Award for Medical Research, which was given to Dr. C. Walton Lillehei, Dr. Richard L. Varco, Dr. Morley Cohen, and Dr. Herbert Warden, all members of our Department of Surgery, for their "brilliant and imaginative studies which have clarified many of the problems of surgery within the heart."

Three former Minnesotans, Mrs. Lucile Petry Leone, Miss Pearl McIver, and Miss Margaret Arnstein, all of whom entered the United States Public Health Service from the University of Minnesota, also received a Lasker Award for distinguished leadership in the development of public health nursing services which "have significantly furthered the interests of public health and made a notable contribution to the advancement of the well-being of this country."

Within the Laboratory Section of the Association, the annual Kimble Award for outstanding contribution to the development of laboratory procedures was presented to Dr. Paul W. Kabler, M.D., University of Minnesota, 1938.

Another prominent Minnesotan, Senator Hubert H. Humphrey, spoke on "The United States and International Health" at a large luncheon meeting arranged by the National Citizens Committee for the World Health Organization. At this same meeting, it was my privilege to report on the Eighth World Health Assembly which was held in Mexico City last May. Also, at this meeting, Dr. James E. Perkins, M.D., University of Minnesota, 1930, Managing Director of the National Tuberculosis Association, spoke on "World Health Goals in Tuberculosis Control."

In addition to the above, many other Minnesotans made prominent contributions to the meeting as speakers on the program, as officers of sections, and chairmen or members of important committees. This was truly an important national meeting in which Minnesotans can take real and justifiable pride.

HAROLD S. DIEHL, M.D.

*Dean of Medical Sciences, University of Minnesota*

# In Memoriam

## ALBERT JUSTUS CHESLEY

Dr. Albert J. Chesley, secretary and executive officer of the Minnesota State Board of Health, died in St. Mary's Hospital, Rochester, October 17, 1955. Born in Minneapolis in 1877, he spent a lifetime working in and for the State of Minnesota.

Dr. Chesley was a life member of the Hennepin County Medical Society and the Minnesota State Medical Association. He was a fellow of the American Medical Association and a member of the Joint Committee on Health Problems in Education. He was also a member of the Association of Military Surgeons of the United States, the American Epidemiological Society, on the board of directors of the American Child Health Association, an honorary life member of the American Social Hygiene Association. He was an honorary fellow of Britain's Royal Sanitary Institute and worked with many other groups, including the National Society for the Prevention of Blindness, the Veterans of Foreign Wars, the Order of Masons and Nu Sigma Nu fraternity.

Among many honors, Dr. Chesley was holder of the Outstanding Achievement Medal of the University of Minnesota, and the Distinguished Service Medal of the Minnesota State Medical Association.

He is survived by his wife; a daughter, Mrs. Paul Miller of Minneapolis; and two grandchildren.

Following are excerpts from the story on Dr. Chesley in *Minnesota's Health*, monthly publication of the State Department of Health, November, 1955.

Dr. Chesley was appointed secretary and executive officer of the board on May 13, 1921, and in all that time he had attended every meeting of the board. Active almost to the end, the way he would have wanted it, he died October 17 at age seventy-eight.

At the outbreak of the Spanish-American War, Dr. Chesley added a year to his age to enlist as a private in the medical corps of the U. S. Army, and was sent to the Philippines. There he served as a medical aide for the wounded in the field and volunteered for duty in special hospitals, particularly those for smallpox and Hansen's disease.

It was on his return from the Philippines that he began his long public health career in Minnesota. He started in 1901 as a clerk in the state health department, and worked part time as a laboratory assistant while completing his medical education at the University of Minnesota. When he received his medical degree in 1907 he was appointed an assistant bacteriologist.

He is believed to have had the longest continuous record of public health work in the nation. With the exception of the period from May 1918 to October 1920, he served his entire public health career in his native state. When World War I broke out he was held in the United States as long as he would submit to it. He reached Europe as a public health expert for the American Red Cross, Commission to France, and later

was chief of staff, American Red Cross, Commission to Poland. It was overseas that he met and married his wife, then Dr. Placida Gardner, a member of his staff.

Dr. Chesley had become director of the division of preventable diseases by the time he went overseas. Shortly after his return from Poland, Dr. Chesley found himself acting secretary and executive officer. Upon the death of Dr. Smith, then executive officer, Dr. Chesley, aged forty-four, succeeded to the office and became the state's fourth health officer, on May 3, 1921.

Dr. Chesley was always true to the obligation he had assumed to protect and preserve the health of the people of Minnesota. In his lifetime he had lived through some of the great epidemics, had seen many of these diseases brought under control, and he himself had played an active part in the battle against them. Changing conditions brought new health problems. Work ceased in some areas and expanded in other directions as advances were made in the knowledge of how to combat disease. To each problem and to each advance, Dr. Chesley gave the benefit of his knowledge, his time, and his sincere interest. At the same time he was quick to point out that the only "new" thing about many of the so-called new problems was a willingness to do something about them.

Lack of funds was an obstacle but it did not deter him. The first legislative appropriation for the department had been in the amount of \$500. He had worked with men who got things done in spite of budget limitations. On more than one occasion in the early days he forfeited his own modest salary to keep a program going where he felt there was a need but for which funds were not available.

Most of the recommendations made in his first biennial report have been carried out, although some of them were slow in coming. As the result of the tuberculosis control program, in which he maintained a continuous interest, he saw the tuberculosis death rate fall from 69.95 per 100,000 in 1922, with 1,726 deaths, to a rate of 4.4 with only 138 deaths in 1954.

A section of industrial health was set up in the health department in 1943 after the adoption of a general code for environmental sanitation by the State Industrial Commission. The section of water pollution control was organized in 1945 following the enactment of the State Water Pollution Control Act. By law, the secretary and executive officer of the state board of health is secretary of that commission and the technical aspects of its work are carried out by the health department.

Dr. Chesley had a real love for children and a deep concern for their health. The results of his program of maternal and child health are indicated by the current infant and maternal mortality rates. In 1954, it was calculated that 419 Minnesota mothers and 5,650 infants lived that year who would have died had 1915 mortality rates prevailed.

"Children never had a better friend nor did the Chil-

## IN MEMORIAM

dren's Bureau," wrote Dr. Martha M. Eliot, chief of the Children's Bureau, on his death. In the words of Katharine F. Lenroot, former chief of the bureau, he was "a great pioneer in child health as well as general health. I always take pride especially in his service to Indian children."

One of the problems of deepest personal concern to Dr. Chesley was the improvement of health services for Indians. His ingenuity in bringing the subject of Indian health into almost any public or private health discussion was incredible. Visitors could almost measure the degree of welcome he extended to them by the length of time that passed before he made some reference to the Indians. Many of his Indian friends, knowing his concern for them and his love of children, named their sons, "Chesley" and he was proud of it.

The record is impressive. Minnesota was the first state to employ an Indian public health nurse on a reservation. In 1924 an old frame Indian school by Leech Lake was converted into the Onigum Tuberculosis Sanatorium. The state held its first general Indian health clinic in 1929 at which over 700 Chippewas who had come to harvest wild rice received physical examinations. In 1936, one year after the opening of the 125-bed Chippewa wing at the State Sanatorium, the tuberculosis death rates per 100,000 among Minnesota Indians was 385. For Dr. Chesley, 1954 was memorable—for the first time on record in Minnesota, no Indian deaths from tuberculosis were reported. The transfer this year of Indian health and medical care from the Bureau of Indian Affairs to the Public Health Service was almost entirely due to his efforts.

He saw the need for public health nurses with special training to fit them for their work with families. As early as 1917, when he was director of the division of preventable diseases, he claimed that "such nurses should themselves be teachers." Throughout his career he worked for the development of good public health nursing services for all parts of the state.

Dr. Robert N. Barr, who succeeds Dr. Chesley as secretary and executive officer, was one of his "boys." There are at least fifty health officers and others holding important posts in public health throughout the country who can proudly make that claim.

In 1937, Dr. Chesley initiated the first field training course in the middlewest for health officers, a course that was a forerunner of the school of public health at the University of Minnesota. He himself was a professor of public health in the department of preventive medicine at the University for 20 years, 1925-1945.

Dr. Chesley took both professional and personal pride in the outstanding research and training programs of the University of Minnesota medical school. Dr. Harold S. Diehl, dean of the school, had been one of the "bright young men" on his staff in Poland. Dr. Chesley's leadership, interest, and support of the program in public health at the University was a prime factor in the establishment of the school of public health. To perpetuate that personal interest and concern, friends are now contributing to what is to be the Albert J.

Chesley memorial fund for a lectureship in public health, to be handled through the Greater University Fund.

Although he did his major work in Minnesota, Dr. Chesley belonged as much to the nation as to the state. When he received the distinguished service medal of the Minnesota State Medical Association in 1948, it was for "outstanding service in the field of public health and social hygiene, not only in Minnesota but elsewhere in the United States and abroad; and for his rare insight and fine understanding of the private practice of medicine to which, as one of its most ardent associates, he has given unfailing co-operation at all times."

Nearly every honor that exists in public health had been awarded to Dr. Chesley. The last was announced at the eighty-third annual meeting of the American Public Health Association when he was named the recipient of the annual Sedgwick Memorial Medal. The occasion was to have been "a special opportunity for recognition of our admired friend," wrote Dr. Reginald M. Atwater, executive secretary of the association of which Dr. Chesley had been president in 1930.

The last tribute paid to him during his lifetime came from the state in which he was born on September 12, 1877, from which he had received his education, and in which he had done his work. Only four days before his death, he was elected an honorary member of the Wabasha County Medical Society at its eighty-seventh annual meeting.

He was president of the State and Provincial Health Authorities from 1924 to 1927 and secretary from 1927 to 1945, when the group finally accepted the resignation he submitted annually.

He was equally active in the Association of State and Territorial Health Officers. "The meetings will never be the same without this wonderful friend and public servant," wrote Dr. Bruce Underwood, commissioner of health in Kentucky.

Only one who had lived public health with him could list the many accomplishments in health fields to which he gave leadership, guidance, and assistance but for which he gave the credit to others. He was a modest man and preferred not to be in the limelight. He had a terrific loyalty to his staff.

The lights burned at all hours in his office in the health department. He did not spare himself and it was hard for him to understand why others were not at their desks on holidays or over week-ends. Time was of no moment to him. Those who knew him best can recall few occasions when he took a vacation.

The long hours he spent on his job kept him in touch with what was happening in public health. Up to the very last, he knew everything that was going on in the building, in the state, and in the nation. He was a crusader and a fighter who held fast for the things in which he believed. Those who knew him best also remember his warmth and gentleness, his quiet sense of humor, and his many, many thoughtful deeds.

"Minnesota stands out among all the states in the country for its progress in public health and largely

*(Continued on Page 952)*

# Reports and Announcements

## MEDICAL MEETINGS

### National

Congress on Industrial Health, 16th annual meeting, Sheraton-Cadillac Hotel, Detroit, Michigan, January 23-24, 1956.

American College of Surgeons, sectional meeting, Hotel Schroeder, Milwaukee, Wisconsin, February 27-29, 1956. Dr. Forrester W. Raine, Milwaukee, chairman.

Atlanta Graduate Medical Assembly, Biltmore Hotel, Atlanta, Georgia, February 20-22, 1956.

Mediclinics of Minnesota, postgraduate course sponsored by Academy of General Practice of Broward County, Fort Lauderdale, Florida, March 5-14, 1956.

## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next scheduled examination (Part 1), written examination and review of case histories, for all candidates for the American Board of Obstetrics and Gynecology will be held in various cities of the United States and Canada on February 3, 1956.

Case abstracts, totalling twenty, are to be sent by the candidate to the secretary, Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland, Ohio, as soon as possible after receiving notification of eligibility for the Part 1 written examination.

## AMERICAN COLLEGE OF SURGEONS

Twelve Minnesota physicians were elected to fellowship in the American College of Surgeons at the annual meeting of the organization in Chicago during the first week of November. The new fellows include Dr. Charles D. Adkins, Dr. Maxwell M. Barr, Dr. Merrill D. Chesler, Dr. Conrad I. Karleen and Dr. D. Keith Millett, all of Minneapolis; Dr. Henry W. Dodge, Jr., Dr. F. Henry Ellis, Jr., and Dr. Edward D. Henderson, all of Rochester; Dr. William C. Downing, Crookston; Dr. Kenneth A. Storsteen, Duluth; Dr. John R. Nickerson, Fairmont, and Dr. Robert P. Meyer, Faribault.

## CONTINUATION COURSES

The University of Minnesota announces a continuation course in *Emergency Surgery for General Physicians* which will be presented at the center for Continuation Study from January 30 to February 1, 1956. The management of various types of injuries will be taken up in detail, as will certain other common surgical emergencies. The course will be presented under the direction of Dr. O. H. Wangenstein, professor and chairman, Department of Surgery.

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Neurology will be the subject of a continuation course to be presented by the University of Minnesota at the Center for Continuation Study next February 6 to 10, 1956. Intended primarily for physicians in general prac-

tice, the program will have appeal also for neurologists and neurosurgeons. The most commonly seen neurological symptoms and syndromes will be stressed.

Guest faculty will include Dr. William M. Meacham, associate clinical professor of surgery, Vanderbilt University School of Medicine, Nashville; Dr. Morris B. Bender, director, Neurology Service, Mount Sinai Hospital, and professor of clinical neurology, New York University College of Medicine, New York City; Dr. John F. Sullivan, associate professor and head, Department of Neurology, Tufts College Medical School, Boston, and Dr. Oliver H. Lowry, professor and head, Department of Pharmacology, Washington University School of Medicine, St. Louis.

The course will be presented under the direction of Dr. A. B. Baker, professor and director, Division of Neurology, and Dr. William T. Peyton, professor and director, Division of Neurosurgery, University of Minnesota Medical School.

\* \* \*

The University of Minnesota announces a continuation course in *Recent Advances in Internal Medicine for Internists* which will be held at the Center for Continuation Study from February 13 to 15, 1956. This year's program will deal principally with recent advances in the fields of endocrinology and metabolism, renal disease, an cardiology.

Guest speaker will be Dr. Joseph W. Jailer, associate professor, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York City, who will also give the Minnesota Pathological Society Lecture on Tuesday evening, February 14. The course will be presented under the direction of Dr. C. J. Watson, professor and head, Department of Medicine.

\* \* \*

Cancer Detection will be the subject of a continuation course for general physicians which will be presented at the Center for Continuation Study by the University of Minnesota and the Minnesota Division of the American Cancer Society from February 16 to 18, 1956. Cancer detection techniques which can be used effectively in general practice will be stressed. The course will be presented under the direction of Dr. O. H. Wangenstein, professor and chairman, Department of Surgery, and Dr. W. A. Sullivan, director, Cancer Detection Center.

## WABASHA COUNTY SOCIETY

At the eighty-seventh annual meeting of the Wabasha County Medical Society at Plainview on October 6, Dr. B. J. Bouquet, Wabasha, was elected president of the organization. He succeeds Dr. E. W. Ellis of Elgin.

Other officers elected were Dr. D. G. Mahle, Plainview, vice president; Dr. B. A. Flesche, Lake City, secretary-treasurer; Dr. E. C. Bayley, Lake City, delegate to the state association, and Dr. Ellis, alternate.

# Woman's Auxiliary

## STATE AUXILIARY HOLDS FALL MEETING

Mrs. L. J. Leonard, Minneapolis

The pattern of the Fall School of Instruction, held at the Curtis Hotel on Tuesday, October 4, was somewhat different this year. Mrs. H. H. Fesler opened the session with a short business meeting and this was followed by a panel discussion, with Mrs. Peter Rudie as moderator. Members on the panel were the officers and committee chairmen who served last year, and the information and advice they supplied to the new chairmen were invaluable. Mrs. M. I. Hauge spurred each member on to greater achievement by saying, "When you stop being better, you stop being good!"

Mr. Leo Brown, Chicago, Director of the Department of Public Relations, American Medical Association, spoke on the subject, "The Doctor's Wife and Public Relations." Several examples of extremely unfavorable public relations shown by doctors' wives were cited by Mr. Brown, who admitted these were rarities. However, the strongest factor influencing public relations between the doctor and the people in his community is the behavior of the doctor and his wife. He stated that improved patient relationship is the first step toward improved public relations: if improved services are stressed, improved public relations will follow automatically.

He stated that less than 30 per cent of our doctors read the valuable material sent them by the AMA, and suggested that the wives could do some of this reading for their husbands. A new booklet, "To All My Patients," scheduled for mailing to doctors' offices after October 20, Mr. Brown said should be read and not be delegated to the wastebasket. "The Human Side and the Business Side of Medicine" is another AMA pamphlet he recommended.

In closing, Mr. Brown gave the following quotation from Charles Dickens:

"I never walk out with my husband, but I hear the people bless him. I never go into a house of any degree, but I hear his praises, or see them in grateful eyes. I never lie down at night, but I know that in the course of that day he has alleviated pain and soothed some fellow creature in the time of need. I know that from the beds of those who were past recovery, thanks have often, often gone up, in the last hour, for his patient administration. Is not this to be rich? The people even praise ME as the doctor's wife."

Dr. F. W. Behmler, Morris, Minnesota, State Senator and vice president of the Minnesota State Medical Association, gave an inspiring and challenging talk on the dangers lurking ahead through legislative channels: granting osteopaths the right to administer drugs and to perform surgery. He referred to the article on pages 736-742 in the July 2, 1955, issue of *The Journal of the American Medical Association* which gives a clear, concise picture of the situation as it exists today. He advised any women living in communities where the

League of Women Voters is an active group, to join them and participate.

The meeting recessed at 12:30. At 1:00 P. M., a delightful luncheon was served in the Cardinal Room. Mrs. Fesler introduced the guests and also the past state presidents who were present. Dr. H. B. Sweetser brought greetings from the State Medical Association.

Mrs. Mason G. Lawson, Little Rock, Arkansas, National President, spoke in a very sincere and informal manner, with all the charm of the South. She stressed the importance of the individual county member, placing her achievement over that of the national member who sets the policy but does not produce the ultimate results. She is much interested in the promotion of the American Medical Education Foundation and described a way in which her own county is helping this cause. Her county auxiliary has had a card printed conveying a Christmas greeting and stating that a contribution to the AMEF has been made in the purchase of the card. This has been done in the belief that the recipient will appreciate the dual purpose which has prompted the sender to use this type of Christmas card.

Mrs. Fesler adjourned the meeting after reading a short poem entitled "It's up to You," which should have inspired everyone there to do her share of auxiliary work. From general comments heard after the session, it was a most successful and worthwhile day, and thanks are due Mrs. Harvey Beek, who had charge of plans.

## NATIONAL AUXILIARY HOLDS CONFERENCE

Mrs. H. H. Fesler, State President

Mrs. L. P. Howell, Rochester, president-elect, and your state president attended the 12th Annual Conference of State Presidents, Presidents-elect and National Committee Chairmen, November 1-3, 1955, at the Drake Hotel in Chicago.

The meeting was called to order by the national president, Mrs. Mason G. Lawson. The theme of the conference was "Active Leadership in Community Health." The purpose was to exchange information, to pool resources of Auxiliary experience, and to become better acquainted with one another. Members came seeking new ideas and trading information. This was accomplished by small groups getting together for Dutch treat breakfasts.

The presiding officer of the conference was Mrs. Robert Flanders, national president-elect. Panel discussions were held on the nine various Auxiliary activities, followed by a question-and-answer period. Your president was assigned to the Organization Panel on "What would you do to include future members in our program now?"

Guest speakers from the AMA appeared on several panels giving many helpful suggestions and valuable information. Dr. Elmer Hess, AMA President, was a luncheon guest speaker and gave an inspiring message on our American heritage and freedom of thought and power to vote, which is so often neglected.

Dr. Ernest B. Howard, Assistant Secretary of the AMA, discussed social security disability benefits. He said that House file H.R. 7225 amendment, which will come up in the spring, will involve millions of people and its impact on the medical profession in the future is serious. Private insurance companies are 100 per cent against this bill.

The best investment we can make is in safety precautions. Medical research shows the national pattern of cause of injury; 50 per cent of injuries are due to doors on cars popping open and persons falling out. Safety precautions on cars will not develop until the public demands them.

The American Medical Education Foundation is planning an eighty dimes campaign this spring—a dime for each of our eighty-one medical schools in the nation. All over the country, people are calling for more doctors, more research and more health services, but the medical schools are handicapped by lack of funds. They need help now. Contributing to the national fund is a sound way to keep all the schools with a single gift. The need to keep our medical schools free, solvent and progressive, is \$10,000,000 a year.

The final day of the conference, a tour of the AMA, headquarters was held. The program included greetings from Dr. George F. Lull, Secretary and General Manager, and a talk by Dr. Austin Smith, chairman of U. S. Committee, World Medical Association. Dr. Smith said that in the past Europe was the medical center; now the trend is reversed and people are flocking to our country for information and training.

Four excellent health movies were shown, followed by a luncheon at the AMA headquarters, and adjournment.

The reports in full will be printed in the January issue of *The Bulletin*. Please don't fail to read them. It was a most successful and inspiring conference.

#### IN MEMORIAM

##### ALBERT JUSTUS CHESLEY

(Continued from Page 949)

because of his work. His old friends will remember his wisdom, his dedication, and his fine kindness and gaiety as long as they live," wrote R. R. Rosell, executive secretary of the Minnesota State Medical Association.

It is hard to remember how young the state health department is in terms of history or how old it is in terms of public health. It is even harder to believe that one man, in his life span, has personally experienced so much of it. The words of Dr. Hewitt, when he summed up his own career in public health in the annual report of the Minnesota State Board of Health for 1896 apply equally to Dr. Chesley: "The best years of my life and effort have gone into this work. I have spared neither time, labor, nor thought, to make it what it ought to be. Such as it is, the record is made and closed." Dr. Chesley gave his entire life to public health. Few men have done so much so unselfishly for his fellow men.

#### MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

230 Lowry Medical Arts Building  
Saint Paul 2, Minnesota

F. H. Magney, M.D., Secretary

#### MINNEAPOLIS MIDWIFE SENTENCED FOR WILLFULLY MAKING FALSE BIRTH CERTIFICATE

*Re: State of Minnesota vs. Lillian Twedt*

On November 14, 1955, the above-named defendant, sixty-seven, 2246 Benjamin Street, N.E., Minneapolis, a licensed midwife, was sentenced by the Hon. Irving R. Brand, Judge of the District Court of Hennepin County, to a term of six months in the Minneapolis Women's Detention Home on a charge of willfully making a false birth certificate. However, Judge Brand stayed sentence for a period of one year and placed the defendant on probation during that period of time. Mrs. Twedt had originally been charged with a felony, offering false instruments for filing or record, to which she had entered a plea of not guilty in Hennepin County District Court on September 20, 1955, but the charge against her was later reduced to a misdemeanor, the crime of willfully making a false birth certificate, to which she entered a plea of guilty on October 3, 1955 before Judge Brand. At that time, Mrs. Twedt surrendered her midwifery license in open court and also signed an agreement with the Minnesota State Board of Medical Examiners authorizing the Board to permanently cancel her license. She also agreed not to make application to the Board in the future for a license to practice midwifery.

The criminal charge against Mrs. Twedt was based upon a birth certificate which was filed by her in connection with the birth of a baby on March 7, 1955, to an unmarried Minneapolis mother, the defendant having been in attendance at the birth. The birth certificate, which was filed with the Clerk of District Court of Anoka County, Minnesota, contained false information in reference to the place of birth, the names of the parents and other data concerning them, and also in regard to the legitimacy of the child. After the birth of the baby, it was placed in the Richfield, Minnesota, home of the persons who were listed on the birth certificate by Mrs. Twedt as being the father and mother of the child.

Mrs. Twedt, who was born in Saint Paul, Minnesota, on March 4, 1888, was licensed to practice midwifery in Minnesota on March 1, 1932. She holds a diploma dated June 3, 1928, from the Chicago School of Practical Nursing. The Minnesota State Board of Medical Examiners on November 5, 1955, made an order revoking the license to practice midwifery held by Mrs. Twedt.

The best thing to give your enemy is forgiveness; to an opponent, tolerance; to a friend, your heart; to your child, a good example; to a father, deference; to your mother, conduct that will make her proud of you; to yourself, respect; to all men, charity.

—BALFOUR

MINNESOTA MEDICINE

# General Interest

A drive for funds for a million-dollar **Masonic Memorial Cancer Hospital** at the University of Minnesota was launched by 68,000 Masons on November 9. The hospital, which will care primarily for those suffering with advanced stages of cancer, is planned to be located in the grouping of the Mayo Memorial and Variety Club Heart institutions at the University.

\* \* \*

**Dr. Erling W. Hansen**, professor and head of the department of ophthalmology at the University of Minnesota, was named president-elect of the American Academy of Ophthalmology and Otolaryngology at its annual meeting in Chicago on October 13. He will take office in January, 1957, succeeding **Dr. A. C. Furstenberg**, dean of the University of Michigan Medical School, president for 1956.

Elected as a vice president of the organization was **Dr. Henry L. Williams**, Rochester.

\* \* \*

**Dr. Heinz H. Bruhl**, staff member of the Faribault State School and Hospital, was the principal speaker at a meeting of the Faribault Rotary Club on October 19. Dr. Bruhl described his impressions of Europe following a two-month tour of the continent this past summer.

\* \* \*

**Dr. Wesley W. Spink**, professor of medicine at the University of Minnesota, left for Tunisia on November 18, the start of a three-week trip to Africa and Europe, during which he planned to study and lecture on brucellosis.

\* \* \*

**Dr. and Mrs. Merrill D. Chesler**, Minneapolis, returned in October from a two-week vacation in New York and New Jersey, during which Dr. Chesler attended the annual meeting of the American Society of Plastic and Reconstructive Surgery at Atlantic City. On November 8, Dr. Chesler conducted a regional seminar at Union Hospital, New Ulm, speaking on "The Treatment of Burns and Birthmarks in Children."

\* \* \*

At the second annual Veterans of Foreign Wars Cancer Day at the University of Minnesota on October 15, the VFW reported that it has raised \$150,000 of the \$450,000 it needs to found a cancer research clinic at the University. At a luncheon the organization honored **Dr. Owen H. Wangenstein**, chief of the department of surgery at the University.

\* \* \*

**Dr. Wallace R. Anderson**, Austin, spoke on accident prevention at a meeting of the Modern Matrons in Austin on November 3.

\* \* \*

**Dr. John W. Henderson**, Rochester, has been named a section editor for the *Survey of Ophthalmology*, a new bi-monthly journal which will make

its debut in February, 1956. The magazine, which will be published by Williams & Wilkins Company, Baltimore, is under the editorial direction of **Dr. Frank W. Newell**, chairman of the section on ophthalmology at the University of Chicago.

\* \* \*

**Dr. David A. Sher**, Virginia, has been named a deputy county coroner by **Dr. Cyril Smith**, Duluth, coroner of St. Louis County.

\* \* \*

Principal speakers at a meeting of the Minnesota Society of Neurology and Psychiatry in St. Paul on November 8 were **Dr. G. Wendell Hopkins** and **Dr. Maynard M. Cohen**, both of Minneapolis. Dr. Hopkins presented a paper on "Carbon Dioxide Therapy in Psychiatric Patients," while Dr. Cohen spoke on "The Neurologic Research Program at the University of Minnesota." Each presentation was an inaugural thesis.

\* \* \*

At a State Medical Journal Conference at A.M.A. Headquarters in Chicago on November 7 and 8, MINNESOTA MEDICINE was represented on the program by **Dr. Arthur H. Wells**, Duluth, editor-in-chief, and **Olive V. Seibert**, Minneapolis, member of the board of editors of the publication. Dr. Wells gave a talk on "Editorial Boards and Editorial Advisory Committees." Miss Seibert conducted a workshop on editing material for publication in medical journals. The conference was held under the auspices of the Advisory Committee of the State Journal Advertising Bureau.

\* \* \*

**Dr. Thomas B. Magath**, Rochester, has been advanced to the rank of rear admiral in the United States Naval Reserve.

\* \* \*

**Dr. Carl W. Waldron**, Minneapolis, was the subject of a biographical sketch in the Town Toppers column of the *Minneapolis Star* on October 24. Dr. Waldron, who holds both medical and dental degrees, is now in semi-retirement after practicing in Minneapolis since 1919.

\* \* \*

**Dr. Owen G. McDonald**, Duluth, has been elected a member of the board of governors of the American College of Surgeons, to represent Minnesota for the term 1955-1957. He will fill the vacancy caused by the death of **Dr. Howard K. Gray**, Rochester.

\* \* \*

Principal speaker at a meeting of the St. Thomas College and Academy Mothers Club in St. Paul on October 18 was **Dr. Philip K. Arzt**, St. Paul. His topic was "The Psychiatric Aspects of Behavior Problems in Children."

\* \* \*

**Dr. A. B. Hunt**, Rochester, was named president

## GENERAL INTEREST

of the Central Association of Obstetricians and Gynecologists at a meeting of the organization in Columbus, Ohio, October 6 to 8.

\* \* \*

**Dr. Fred W. Wittich**, Minneapolis, president of the International Association of Allergists, left on October 31, for Rio de Janeiro, Brazil, to preside at the second congress of the organization. The meeting, attended by 600 members, was held November 6 through 12.

\* \* \*

Principal speaker at a Parent-Teachers Association meeting in Brainerd on October 18 was **Dr. E. R. Kanne**, Brainerd, who spoke on "Child Health."

\* \* \*

The seventeenth annual award of the American Pharmaceutical Manufacturers Association has been bestowed upon **Dr. Charles W. Mayo**, Rochester, for his "outstanding contributions to both medicine and world understanding." Presentation of the award was scheduled for a dinner in New York on December 13.

Earlier, on October 23, it was announced that **Dr. Mayo** had been elected a trustee of the University of Pennsylvania. An alumnus of Pennsylvania's School of Medicine, **Dr. Mayo** is also a member of the board of regents of the University of Minnesota.

\* \* \*

**Dr. David W. Francis**, Morristown, was given a special attendance award at the fortieth meeting of the Interstate Postgraduate Medical Association at Milwaukee, Wisconsin, November 14 to 17. The award is given to physicians who have contributed to their medical education by attending ten or more meetings of the organization since 1940.

\* \* \*

**Dr. Owen H. Wangenstein**, chief of surgery at the University of Minnesota, has been elected first vice president of the American College of Surgeons.

\* \* \*

**Dr. Robert N. Barr**, deputy executive officer of the Minnesota Health Department since 1949, was named secretary and executive officer of the Minnesota State Board of Health on November 1. He succeeds **Dr. A. J. Chesley**, who died on October 17. **Dr. Barr** has been with the health department since 1934.

\* \* \*

**Dr. N. L. Gault, Jr.**, was named assistant dean of the College of Medical Sciences at the University of Minnesota by the board of regents on October 22. **Dr. Gault**, who has been a member of the medical faculty since 1953, will take over his new duties on January 1, succeeding **Dr. Howard L. Horns**, who has resigned. Also an assistant dean of the medical school is **Dr. William F. Maloney**.

\* \* \*

Principal speaker at a meeting of the West Duluth Women's Club on November 4, was **Dr. George M. Cowan**, Duluth. He discussed the subject, "What Makes Women Nervous?"

An Albert Lasker Award for outstanding achievement in medical research has been given to four University of Minnesota surgeons: **Dr. C. Walton Lillehei**, **Dr. Richard L. Varco**, **Dr. Morley Cohen** and **Dr. Herbert E. Warden**. The award was presented for their numerous advances in cardiac surgery.

\* \* \*

**Dr. Edgar V. Allen**, Rochester, was elected president of the American Heart Association at its annual meeting in New Orleans, Louisiana, recently. **Dr. Allen** has been a member of the board of directors of the organization since 1944.

\* \* \*

**Dr. Harold S. Diehl**, dean of the University of Minnesota College of Medical Sciences, has been elected vice president of the Association of American Medical Colleges for 1956.

\* \* \*

"Pleural Effusion" was the title of a talk given by **Dr. W. R. Schmidt**, Minneapolis, at a dinner meeting of the Southwestern Minnesota Medical Society in Worthington on October 10.

\* \* \*

**Dr. Emil J. Fogelberg**, St. Paul, was named president-elect of the Minnesota Academy of General Practice at the annual meeting of the organization in Minneapolis on October 18. He will succeed **Dr. Raymond Page**, St. Charles, who will serve as president during 1956. Other officers named at the meeting were **Dr. E. J. Tanquist**, Alexandria, vice president, and **Dr. John Butler**, Cloquet, secretary.

Named as new directors of the organization were **Dr. Herbert L. Stolpestad**, St. Paul; **Dr. Paul M. Smith**, Lake Crystal, and **Dr. H. A. Korda**, Pelican Rapids.

\* \* \*

Grants from the American Cancer Society to the University of Minnesota have now exceeded two million dollars for cancer research and training. The announcement was made by **Dr. David P. Anderson**, Austin, retiring president of the society's Minnesota Division, at its annual meeting in Minneapolis on October 14.

Among the new officers elected by the division are **Dr. Lyle J. Hay**, Minneapolis, second vice president, and **Dr. Philip F. Eckman**, Duluth, third vice president.

\* \* \*

**Dr. C. S. Donaldson**, St. Cloud, was named head of the medical services of Civil Defense in St. Cloud at a meeting on October 12. He succeeds **Dr. R. N. Jones** and will have charge of organizing physicians, dentists and nurses.

\* \* \*

**Dr. Miles Griffin**, Oakland, California, was named president of the Alumni Association of the Mayo Foundation at the organization's thirty-first annual meeting in Rochester on October 28. He succeeds **Dr. Shirley C. Lyons** of New Orleans, Louisiana.

Other new officers include **Dr. George E. Rice**,

(Continued on Page xxii)

# Index to Volume 38

## A

- Abbott, William E., Levey, Stanley, Benson, Jerrel W., and Davis, John H.: Alterations of carbohydrate metabolism following trauma, March suppl., 55
- Abdominal aorta, Clinical aspects of arteriosclerotic aneurysm and arteriosclerotic occlusion of the, 836
- Abdominal diseases, acute, Management of, 315
- Abscess, brain, Radical treatment of, 547
- Accident benefit plan, Athletic, 1954-1955, 183
- Accidents, Choking, 235
- Acute pulmonary edema, 605
- Acute renal insufficiency, March suppl., 52
- Adenotonsillectomy, Indications and contraindications for, 458
- Adkins, Galen H., Fahr, George, and Bernstein, Irving C.: Hypertensive encephalopathy versus schizophrenia, 636
- African populations, Arteriosclerosis in, 852
- Alkalosis, Relation of, to potassium deficiency, March suppl., 4
- Alterations of carbohydrate metabolism following trauma, March suppl., 55
- Altschule, Mark D.: Acute pulmonary edema, 605
- Amino acids and sugar, Vehicles and volume, with special reference to, March suppl., 26
- Analgesia, Will (it) evolve from a century of anesthesia? 682
- Anal pruritus, 19
- Anderson, Ray C.: Heredity of diseases of the heart, blood vessels, and blood, 82
- Andrus, E. Cowles: Medical emergencies in myocardial infarction, 888
- Anemia, Hemolytic, 463
- Anemia, The treatment of, 327
- Anesthesia, Influence of, on maternal mortality, 623
- Anesthesia, Will analgesia evolve from a century of? 682
- Aneurysms of arteriosclerotic origin, Surgical treatment of, 922
- Anfinson, Christian B.: Lipoprotein metabolism in the etiology of atherosclerosis, 767
- Anticoagulant therapy, Laboratory control of, 43
- Aorta, abdominal. Clinical aspects of arteriosclerotic aneurysm and arteriosclerotic occlusion of the, 836
- Arhelger, Stuart W., and Gilbertsen, Victor A.: Tetanus, 393
- Ariel, Irving M.: Fluid and electrolyte requirements of the surgical patient as influenced by the post-traumatic response, March suppl., 36
- Armstrong, Wallace D.: Radioisotope studies of the physiology of calcified tissues, 618
- Arterial disease, coronary, Surgical treatment of, 570
- Arterial disease, Occlusive—its management by the use of homografts, 912
- Arterial disease, Occlusive—its management by thromboendarterectomy, 904
- Arterial homografts, Healing and fate of, 916
- Arterial occlusions, segmental, Use of greater saphenous vein autographs in reconstruction of, 918
- Arterial segments, diseased, Plastic replacement of, 927
- Arteriosclerosis, cerebral, Clinical picture of, 839
- Arteriosclerosis, Challenge of, to medical education, 731
- Arteriosclerosis, Challenge of, to surgeons, 902
- Arteriosclerosis, Factors other than cholesterol in, 749
- Arteriosclerosis in African populations, 852
- Arteriosclerosis, occlusive, of the extremities, Clinical aspects of, 829
- Arteriosclerosis, Pleomorphism of the lesions of, 746
- Arteriosclerosis problem, Life insurance looks at the, 736
- Arteriosclerosis, Role of the National Heart Institute in meeting the challenge of, 734
- Arteriosclerosis, Strategy and tactics of research in, 743
- Arteriosclerotic aneurysm and arteriosclerotic occlusion of the abdominal aorta, Clinical aspects of, 836

- Association of intracranial meningioma with pituitary adenoma (case report), 335
- Atherogenesis, Coronary—an endocrine problem? 794
- Atherosclerosis, coronary, Ballistocardiogram in the diagnosis of, 880
- Atherosclerosis, Diet and, 206
- Atherosclerosis, Hormonal factors in the pathogenesis of, 788
- Atherosclerosis, Hypertension and, 784
- Atherosclerosis, Lipoprotein metabolism in the etiology of, 767
- Atherosclerosis problem, The, 755
- Athletic accident benefit plan, 1954-1955, 183
- Aurelius, J. Richards, Peterson, Donald H., and Niknejad, Ismail: Retroperitoneal cavernous hemangioma associated with hemangiomas of the skin in a newborn, 32
- Aust, J. Bradley, and Murphy, Thomas O.: Use of greater saphenous vein autographs in reconstruction of segmental arterial occlusions, 918

## Abstracts

- Aerosol administration of alevaire, (September) xxxix
- Cancer of lip and skin, (November) liv
- Clinical comparison of carbinoxamine maleate, tripelenamine hydrochloride, and bromodiphenhydramine hydrochloride in treating allergic symptoms, (September) xxxvi
- Lung cancer, a "great simulator," (November) lii
- Outlook less grim for childhood cancer, (November) li
- Practical considerations in digitalis therapy, (September) xxxvi
- Use of cobalt and iron in the treatment and prevention of anemia of prematurity, (September) xli
- Use of radioiodine in the study of thyroid disorders, The, (September) xxxv

## American Medical Association

- Proceedings of the House of Delegates, Eighth Clinical Meeting, 56
- Proceedings of the House of Delegates, 104th annual meeting, 511
- Proposed plan of insured endowment for the American Medical Education Foundation, 586

## B

- Bacterial endocarditis, subacute, Present treatment of, 936
- Bahnson, Henry T.: Surgical treatment of aneurysms of arteriosclerotic origin, 922
- Baker, Milton E.: Ectopic pregnancy, 179
- Ballistocardiogram in the diagnosis of coronary atherosclerosis, 880
- Banner, Edward A.: The technique and interpretation of the vaginal examination, 323
- Barr, David P.: Hormonal factors in the pathogenesis of atherosclerosis, 788
- Barr, R. N., Kimball, Anne C., and Bauer, Henry: Serological testing for syphilis in Minnesota, 98
- Barr, Maxwell M., and Sinykin, Melvin B.: Gynecological cancer detection, 174
- Bauer, Henry: Limitations of the Widal test, 189
- Bauer, Henry, Barr, R. N., and Kimball, Anne C.: Serological testing for syphilis in Minnesota, 98
- Beahrs, Oliver H.: Differential diagnosis of tumors of the neck, 293
- Benson, Jerrel W., Davis, John H., Abbott, William E., and Levey, Stanley: Alterations of carbohydrate metabolism following trauma, March suppl., 55
- Berglund, Eldon: Suffocation, a killer of children, 107

# INDEX TO VOLUME 38

- Bergquist, James R., and Sadler, William P.: Polio-  
myelitis complicating pregnancy, 668  
Berkwitz, N. J., Hodges, Allen, and McDermott, Rob-  
ert: Psychiatric out-patient treatment, 633  
Bernstein, Irving C., Adkins, Galen H., and Fahr,  
George: Hypertensive encephalopathy versus schiz-  
ophrenia, 636  
Bilateral glenoid hypoplasia, 568  
Bilka, Paul J.: A new hydrocortisone for intraartic-  
ular use, 408  
Biopsy studies of the gastric mucosa, 268  
Bernstein, William C.: The Southern Minnesota Medi-  
cal Association, 220  
Blackburn, Charles M., and Love, J. Grafton: Assoc-  
iation of intracranial meningioma with pituitary  
adenoma (case report), 335  
Bloch, Henry S.: Chronic hypervitaminosis A, 627  
Blood coagulation, 571  
Blood transfusions and plasma volume expanders, March  
suppl., 48  
Blood vessels, and blood, Heredity of diseases of the  
heart, 82  
Blood volume studies in gastrointestinal hemorrhage, 172  
Boies, Lawrence R.: Choking accidents, 235  
Bone, Diagnostic enigmas of diseases of, 111  
Bowel, Complete obstruction of the, in the newborn, 165  
Boyd, G. S., and Oliver, M. F.: Coronary atherogenesis  
—an endocrine problem? 794  
Boyden, Edward A.: Observations on the history of  
the bronchopulmonary segments, 597  
Brain abscess, Radical treatment of, 547  
Brock, John F., and Bronte-Stewart, B.: Arteriosclero-  
sis in African populations, 852  
Broker, H. M., and Hay, L. J.: Hemobilia following  
blunt trauma to the liver (case report), 333  
Bronchopulmonary segments, Observations on the his-  
tory of the, 597  
Bronte-Stewart, B., and Brock, John F.: Arterio-  
sclerosis in African populations, 852  
Brown, E. B., Jr., and Miller, Fletcher: Clinical im-  
portance of hypercapnia, 602  
Brunsting, Louis A.: Neurodermatitis, 291  
Buchstein, Harold F.: Radical treatment of brain ab-  
scess, 547  
Buie, Louis A.: The heritage of ethics in medicine, 691  
Burnham, Wesley H.: Fractures of the elbow, 16

## Book Reviews

- American Industrial Hygiene Association: Hygienic  
guides, (November) 1  
American Public Health Association: Health supervi-  
sion of young children, 140  
Anderson, W. A. D.: Synopsis of pathology, (Decem-  
ber) xxiv  
Bailey, Hamilton: Demonstrations of physical signs in  
clinical surgery, (November) xliii  
Bauer, Louis H. (editor): Seventy-five years of medi-  
cal progress, 1878-1953, (December) xxiv  
Benford, Robert J.: Doctors in the sky, 530  
Buchanan, Sheena H.: The health visitor and tubercu-  
losis, 290  
Davis, Helen Miles (editor): Science exhibits, (No-  
vember) xlv  
Goldzieher, Max A., and Goldzieher, Joseph W.: Endo-  
crine treatment in general practice, 449  
Last, Raymond Jack: Anatomy; regional and applied,  
290  
Lichtenstein, Louis: Bone tumors, 357  
Link, Mae Mills, and Coleman, Hubert A.: Medical  
support of the army air force in World War II,  
(December) xxv  
Mayo, Charles W.: Surgery of the small and large in-  
testine, 730  
Moore, Frederick J., Cramer, Frank B., and Knowles,  
Robert G.: Statistics for medical students and in-  
vestigators in the clinical and biological sciences, 450

- Pickering, G. W. (chairman): Ciba Foundation sym-  
posium on hypertension, (November) xlvii  
Sarnat, Bernard G. (editor): The temporomandibular  
joint, 357  
Sears, Thad P.: The physician in atomic defense, 449  
Smith, Rodney, (editor): Progress in clinical sur-  
gery, 449  
Strachan, Clarice B.: The diabetics cookbook, (Sep-  
tember) xxxiv  
Titus, Paul (revised by J. Robert Willson): Manage-  
ment of obstetric difficulties, (November) xlv  
Vaughan, Warren T.: Primer of allergy; a guidebook  
for those who must find their way through the  
mazes of this strange and tantalizing state, 357  
Wilder, Lucy: The Mayo Clinic, 596  
Wolstenholme, G. E. W.: Peripheral circulation in  
man: a Ciba Foundation symposium, 450

## C

- Calcified tissues, Radioisotope studies of the physiology  
of, 618  
Cancer detection, Gynecological, 174  
Cancer mortality in Minneapolis, Minnesota, A study  
of, 551  
Cancer of the lung, Cytologic studies in the diagnosis of,  
704  
Cancer of the thyroid, 468  
Can we further decrease infant mortality? 559  
Carbohydrate metabolism, Alterations of, following trau-  
ma, March suppl., 55  
Carcinoma *in situ* of the uterine cervix, 331  
Carcinoma of the common duct, 28  
Carcinoma of the penis, Giant condyloma (verruca)  
simulating, 423  
Cardiac and general surgery, Hypothermia in, 77  
Cataract operations, unilateral, Visual problems of pa-  
tients who have, 420  
Cerebral arteriosclerosis, Clinical picture of, 839  
Cervix, uterine, Carcinoma *in situ* of the, 331  
Challenge of arteriosclerosis to medical education, 731  
Challenge of arteriosclerosis to surgeons, 902  
Chao, Thaddeus M.: The drug therapy of hypertension,  
489  
Children, Fractures of the upper extremity in, 296  
Children, Suffocation, a killer of, 107  
Choking accidents, 235  
Cholangiography, 233  
Cholesterol, Factors other than, in arteriosclerosis, 749  
Cholesterol metabolism, 779  
Christensen, Norman A.: A practical approach to the  
treatment of tetanus, 397  
Chronic hypervitaminosis A, 627  
Clinical aspects of arteriosclerotic aneurysm and ar-  
teriosclerotic occlusion of the abdominal aorta, 836  
Clinical aspects of fluid and electrolyte management, 153  
Clinical aspects of occlusive arteriosclerosis of the ex-  
tremities, 829  
Clinical importance of hypercapnia, 602  
Clinical observations related to pulmonary eosinophilia,  
128  
Clinical picture of cerebral arteriosclerosis, 839  
Coagulation, Blood, 571  
Colitis, ulcerative, Psychiatric aspects of, 86  
Colon and rectum, Tumors of the, 401  
Complete obstruction of the bowel in the newborn, 165  
Condyloma, Giant (verruca) simulating carcinoma of  
the penis, 423  
Coronaries through the ages, The, 801  
Coronary arterial disease, Surgical treatment of, 570  
Coronary atherogenesis—an endocrine problem? 794  
Coronary atherosclerosis, Ballistocardiogram in the diag-  
nosis of, 880  
Coronary heart disease, Diagnosis of, 55  
Coronary heart disease, Electrocardiogram in, 871  
Coronary heart disease, Evaluation of status and re-  
sults of management in, 891

- Coronary heart disease, Mode of life and the prevalence of, 758  
 Cortisone, Precautions in the use of, for treatment of rheumatic diseases, 304  
 County medical society, The, 665  
 Cytologic studies in the diagnosis of cancer of the lung, 704  
 Cytology, Exfoliative: a realistic appraisal, 812

# Clinical-Pathological Conferences

- Adenocarcinoma of the prostate with multiple metastases, 113  
 Leutic aortitis and aneurysm, 194

# Current Cardiac Concepts

- Diagnosis of coronary heart disease, 55  
 Diet and atherosclerosis, 206  
 Iatrogenic heart disease, 348, 432  
 Present treatment of subacute bacterial endocarditis, 936  
 Prophylaxis of rheumatic fever, 702  
 Surgical treatment of coronary arterial disease, 570  
 Use of quinidine in clinical medicine, The, 499  
 Value of the electrocardiogram in diagnosis, The, 640

# D

- Dahlin, David C.: Carcinoma in situ of the uterine cervix, 331  
 Darrow, Daniel: Relation of alkalosis to potassium deficiency, March suppl., 4  
 Davis, John H., Abbott, William E., Levey, Stanley, and Benson, Jerrel W.: Alterations of carbohydrate metabolism following trauma, March suppl., 55  
 Dawson, James R., Jr.: The pathogenesis of hyaline membrane disease of the newborn, 514  
 Death in utero, 701  
 Deaths, Sudden, apparently unexplained, during infancy, 41  
 Delivery, Inversion of the uterus immediately following, 700  
 Development and correction of electrolyte disturbances associated with salt retention, March suppl., 21  
 Diabetes insipidus and pregnancy, 809  
 Diagnosis of coronary heart disease, 55  
 Diagnosis of pancreatitis by laboratory methods, The, 430  
 Diagnostic enigmas of diseases of bone, 111  
 Diamox, 184  
 Diet and atherosclerosis, 206  
 Differential diagnosis of tumors of the neck, 293  
 Digestive ailments of older patients, 309  
 Dockerty, Malcolm, B.: Functioning ovarian tumors, 245  
 Dodds, Thelma: Facts about nursing in Minnesota, 38  
 Drug therapy of hypertension, The, 489  
 Duct, common, Carcinoma of the, 28  
 Duryea, Marbry, Larson, Donald M., Hauge, E. T., and McKenzie, Charles H.: Inversion of the uterus immediately following delivery, 700  
 Duryea, A. Wilbur: Clinical aspects of occlusive arteriosclerosis of the extremities, 829  
 Dwan, Paul F.: Prophylaxis of rheumatic fever, 702

# The Dean's Page

- Dean's page, The, 50  
 Distinguished scientists join faculty, 121  
 Fall semester begins, The, 822  
 Family physician, The, 442  
 Minnesota graduates in public health work, 947  
 Procurement of animals for research, The, 251  
 Undergraduate education for general practice, 201

# E

- Ectopic pregnancy, 179  
 Education, medical, Challenge of arteriosclerosis to, 731  
 Elbow, Fractures of the, 16  
 Electrocardiogram in coronary heart disease, 871  
 Electrocardiogram, The value of the, in diagnosis, 640  
 Electrocardiography, Quantitative, 874  
 Electroconvulsive therapy, Value of succinylcholine chloride in, 1  
 Electrolyte disturbances associated with salt retention, Development and correction of, March suppl., 21  
 Electrolyte disturbances, The milliequivalent as a unit of measure in the interpretation and correction of, March suppl., 1  
 Electrolyte management, fluid and, Clinical aspects of, 153  
 Electrolyte problems, Pediatric, March suppl., 9  
 Electrolyte requirements, Fluid and, of the surgical patient as influenced by the post-traumatic response, March suppl., 36  
 Elman, Robert: Vehicles and volume, with special reference to amino acids and sugar, March suppl., 26  
 Emmett, John L.: Hematuria, 320  
 Encephalopathy, Hypertensive, versus schizophrenia, 636  
 Endocarditis, subacute bacterial, Present treatment of, 936  
 Enigmas in lymphoma, 674  
 Eosinophilia, pulmonary, Clinical observations related to, 128  
 Erickson, Donald J.: Physical therapy for painful shoulder, 556  
 Estrogen, Urinary, and serum protein-bound iodine levels, 800  
 Ethics in medicine, The heritage of, 691  
 Evaluation of status and results of management in coronary heart disease, 891  
 Exfoliative cytology: a realistic appraisal, 812  
 Extremities, Clinical aspects of occlusive arteriosclerosis of the, 829

# Editorial

- Accidents, a killer of old and young, 250  
 Accidents, the killer of children, 120  
 Ancilla,—ae, f. *dim.*, 817  
 Annual meeting, 200  
 BMD, 341  
 Business prospects for 1955, 581  
 Child psychiatry, 199  
 College health services, 709  
 Communication: an overview, 939  
 Consulting psychiatrist "speaks," The, 708  
 Democratic way, The, 707  
 Design and decoration for the doctor's office, 816  
 Diabetes detection programs, 343  
 Diabetic patient and his chest x-ray, The, 433  
 Doctor and the press, The, 501  
 Doctor as a witness in industrial courts, The, 118  
 Drownings—a killer of Minnesotans, 436  
 Family agency and marital counselling, The, 940  
 Family service—what is it? 643  
 Farm prices, 342  
 Flexible farm prices, 435  
 Freedom for philanthropy, 643  
 Function of the Hill Family Foundation, The, 708  
 Function of the state insurance commission, 580  
 General practice residency, 436  
 General practice symposium, 341  
 Harofé Haivri, 434  
 Health examinations, 578  
 Histoplasmosis in Minnesota, 250  
 How a local banker may serve the physician, 249  
 How long should one keep valuable papers? 343  
 "I'm not marrying your mother", 45  
 Life insurance applicant examinations, 45  
 Life insurance in a physician's estate planning, 579  
 Loss of hearing in children, 343

# INDEX TO VOLUME 38

Management of the federal debt, 433  
 Minnesota poll, 248  
 Motor vehicle accidents—A killer of Minnesota children, 506  
 National Association of Boards of Pharmacy, 504  
 "New occasions teach new duties," 119  
 Physical medicine, 814  
 Physician and his business insurance, The, 118  
 Physician and the death certificate, The, 581  
 Poliomyelitis vaccination in Minnesota, 710  
 Present status of the ballistocardiograph, The, 648  
 Psychiatric consultation in social agencies, 814  
 Psychometric measurements, 706  
 Radio-isotopes in medicine, 46  
 Reinsurance is not reassurance, 649  
 Rorschach test, The, 505  
 Separate fund-raising, 815  
 Sigmoidoscopic examinations, 119  
 Savings and loan investment, The, 47  
 Science reporter, The, 436  
 Social Security disability "freeze" provisions, 506  
 Specialty of otolaryngology, The, 579  
 Specialty training in allergy, 342  
 Stall the executive heart attack, 644  
 Status of neurologic research, The, 248  
 Suburban medical migration, 941  
 Taking notes at medical meetings, 197  
 Training laboratory aides, 504  
 Trend or more, A? 942  
 Tuberculosis control in the schools of Minnesota, 939  
 Utilities as an investment, 647  
 Value of a safety deposit box, 200  
 Value of specialty boards, The, 198  
 Venereal disease still a problem, 706

## F

Factors other than cholesterol in arteriosclerosis, 749  
 Facts about nursing in Minnesota, 38  
 Fahr, George, Bernstein, Irving C., and Adkins, Galen H.: Hypertensive encephalopathy versus schizophrenia, 636  
 Faith, Three beginnings, founded in the, 696  
 Fansler, Walter A., and Smith, William T.: Tumors of the colon and rectum, 401  
 Finkelnburg, William O.: Carcinoma of the common duct, 28  
 Fisher, Isadore, and Haas, C. F.: Giant condyloma (verruca) simulating carcinoma of the penis, 423  
 Fisher, Miller: Clinical picture of cerebral arteriosclerosis, 839  
 Fluid and electrolyte management, Clinical aspects of, 153  
 Fluid and electrolyte requirements of the surgical patient as influenced by the post-traumatic response, March suppl. 36  
 Foibles and pitfalls in obstetric hemorrhage, 685  
 Fortier, G. M. W.: Cholangiography, 233  
 Fowler, Ward S.: Pulmonary-function tests, 599  
 Fox, James Rogers: "Ideal" socialized medicine, 538  
 Fractures of the elbow, 16  
 Fractures of the pelvis, 563  
 Fractures of the upper extremity in children, 296  
 Frantz, Ivan D., Jr.: Cholesterol metabolism, 779  
 Frykman, Howard M.: Anal pruritus, 19  
 Functioning ovarian tumors, 245

## G

Gaard, Richard C.: Preoperative use of a combination of levo-dromoran tartrate and a new narcotic antagonist, 637  
 Gall, Edward A.: Enigmas in lymphoma, 674  
 Gastric mucosa, Biopsy studies of the, 268  
 Gastric resection, Psychiatric illness following, 226  
 Gastrointestinal hemorrhage, Blood volume studies in, 172

Giant condyloma (verruca) simulating carcinoma of the penis, 423  
 Gibbs, Robert W.: Complete obstruction of the bowel in the newborn, 165  
 Gilbertsen, Victor A., and Arhelger, Stuart W.: Tetanus, 393  
 Goltz, Robert W.: Topical hydrocortisone in the treatment of skin diseases, 404  
 Gowan, L. R.: Psychiatric aspects of ulcerative colitis, 86  
 Gunlaugson, F. G., Roberts, Jean, and Lundeberg, Karl R.: A study of cancer mortality in Minneapolis, Minnesota, 551  
 Gynecological cancer detection, 174

## H

Haas, C. F., and Fisher, Isadore: Giant condyloma (verruca) simulating carcinoma of the penis, 423  
 Hagen, Paul S.: Hemolytic anemia, 463  
 Hall, Wendell H.: Present treatment of subacute bacterial endocarditis, 936  
 Hammarsten, James F.: Blood transfusions and plasma volume expanders, March suppl. 48  
 Hammes, E. M., Jr.: Puerperal psychoses, 223  
 Hand, Management of recent injuries of the, 299  
 Hartmann, John R.: Water safety for Minnesotans, 428  
 Hauge, E. T., McKenzie, Charles H., Duryea, Marbry, and Larson, Donald M.: Inversion of the uterus immediately following delivery, 700  
 Hay, L. J., and Broker, H. M.: Hemobilia following blunt trauma to the liver (case report), 333  
 Hay, Lyle J., and Owens, Frederick, Jr.: Transplantation of duct of Wirsung in chronic pancreatitis, 411  
 Hazel, Ronald S.: Medical partnerships, 93  
 Healing and fate of arterial homografts, 916  
 Hearing loss in children, 5  
 Heart, blood vessels, and blood, Heredity of diseases of the, 82  
 Heart disease, coronary, Diagnosis of, 55  
 Heart disease, coronary, Electrocardiogram in, 871  
 Heart disease, coronary, Evaluation of status and results of management in, 891  
 Heart disease, coronary, Mode of life and the prevalence of, 758  
 Heart disease, Iatrogenic, 348, 432  
 Heller, Ben I.: Acute renal insufficiency, March suppl. 52  
 Helmer, O. M.: The milliequivalent as a unit of measure in the interpretation and correction of electrolyte disturbances, March suppl. 1  
 Hemangioma, Retroperitoneal cavernous, associated with hemangiomas of the skin in a newborn, 32  
 Hematuria, 320  
 Hemobilia following blunt trauma to the liver (case report), 333  
 Hemolytic anemia, 463  
 Hemorrhage, gastrointestinal, Blood volume studies in, 172  
 Hemorrhage, obstetric, Foibles and pitfalls in, 684  
 Hensel, Charles N.: Iatrogenic heart disease, 348, 432  
 Heredity of diseases of the heart, blood vessels, and blood, 82  
 Heritage of ethics in medicine, The, 691  
 Hexamethonium-induced hypotension, 573  
 Hines, Edgar A., Jr.: Clinical aspects of arteriosclerotic aneurysm and arteriosclerotic occlusion of the abdominal aorta, 836  
 Histoplasmosis, 531  
 Hodges, Allen, McDermott, Robert, and Berkwitz, N. J.: Psychiatric out-patient treatment, 633  
 Hoffman, Olive, Sobel, Harry, Starr, Paul, and Marmorston, Jessie: Urinary estrogen and serum protein-bound iodine levels, 800  
 Holmberg, Conrad J.: Labyrinthine hydrops, 414  
 Homografts, arterial, Healing and fate of, 916

# INDEX TO VOLUME 38

Homografts, Occlusive arterial disease—its management by the use of, 912  
 Hormonal factors in the pathogenesis of atherosclerosis, 788  
 Hufnagel, Charles A.: Occlusive arterial disease—its management by the use of homografts, 912  
 Hurwitz, Milton M.: Diagnosis of coronary heart disease, 55  
 Hyaline membrane disease of the newborn, The pathogenesis of, 514  
 Hydrocortisone, A new, for intra-articular use, 408  
 Hydrocortisone, Topical, in the treatment of skin diseases, 404  
 Hydrops, Labyrinthine, 414  
 Hypercapnia, Clinical importance of, 602  
 Hypercholesteremia, Treatment of, 864  
 Hyperglycemia, Hyperpotassemia and, 565  
 Hyperpotassemia and hyperglycemia, 565  
 Hypertension and atherosclerosis, 784  
 Hypertension, The drug therapy of, 489  
 Hypertensive encephalopathy versus schizophrenia, 636  
 Hypervitaminosis A, Chronic, 627  
 Hypoplasia, Bilateral glenoid, 568  
 Hypotension, Hexamethonium-induced, 573  
 Hypothermia in cardiac and general surgery, 77  
 Hysterectomies, 451

## History of Medicine in Minnesota

Pioneer doctors of Chippewa County prior to the year 1900, 59, 276, 519, 719

## I

Iatrogenic heart diseases, 348, 432  
 "Ideal" socialized medicine, 538  
 Idiopathic pleural effusion, 613  
 Indications and contraindications for adenotonsillectomy, 458  
 Infancy, Sudden apparently unexplained deaths during, 41  
 Infant mortality, Can we further decrease? 559  
 Infarction, myocardial, Medical emergencies in, 888  
 Influence of anesthesia on maternal mortality, 623  
 Intestinal obstruction due to inflammatory strictures, 481  
 Intra-articular use, A new hydrocortisone for, 408  
 Inversion of the uterus immediately following delivery, 700  
 Iodine levels, serum protein-bound, Urinary estrogen and, 800  
 Ivins, John C.: Fractures of the upper extremity in children, 296

## In Memoriam

Abbott, William Pitt, 588  
 Aitkens, Herbert Baker, 588  
 Arling, Philip A., 724  
 Arko, Joseph Lawrence, 724  
 Aurand, William Henry, 588  
 Beise, Rudolph A., 352  
 Bennion, Percival Hale, 656  
 Benoit, Frank Tancrede, 282  
 Berghs, Lyle V., 132  
 Bergquist, Karl Emil, 132  
 Benjamin, Arthur Edwin, 128  
 Boeckmann, Egil, 724  
 Branton, Alloys F., 656  
 Campbell, Robert Allen, 132  
 Campbell, Robert Wilson, 132  
 Carroll, William C., 282  
 Chesley, Albert Justus, 948  
 Ferguson, James Cory, 352  
 Fleming, Aloysius Stephen, 210  
 Friedman, Jack, 817  
 Frost, Edward Harold, 525  
 Galloway, John D. B., 445

DECEMBER, 1955

Ghent, Charles Harry, 210  
 Goeckerman, William H., 67  
 Gray, Howard Kramer, 724  
 Grinnell, Wendell B., 525  
 Haines, James Harris, 282  
 Hallberg, Charles Albert, 210  
 Haugseth, Enoch, 133  
 Havel, Harold William, 656  
 Helland, Gustav M., 133  
 Johnson, Ray George, 210  
 Karn, Bert R., 133  
 Kirk, George P., 210  
 Libert, John N., 725  
 McBroom, David Edward, 726  
 McCann, Eugene John, 726  
 Madden, John Francis, 282  
 Miller, William Anthony, 445, 525  
 Norman, John Francis, 67  
 O'Donnell, Dennis Michael, 133  
 O'Leary, Paul Arthur, 588  
 Peterson, Alfred Carlton, 282  
 Rokala, Henry Emil, 656  
 Rosander, Phyllis E., 525  
 Rowe, William Henry, 67  
 Seljeskog, Sigsbee Raymond, 726  
 Sherman, Hubert Townsend, 352  
 Smith, Leon Grant, 136  
 Sterner, Ernest G., 284  
 Tingdale, Carlyle, 726  
 Wilkinson, Stella Lucy, 656

## J

Johnson, Victor: Three beginnings, founded in the faith, 696  
 Jorgens, Joseph, and Kasper, Robert E.: Bilateral glenoid hypoplasia, 568

## K

Kamman, Gordon R., and Raudenbush, David W.: Medico-legal relations, 228  
 Kasper, Robert E., and Jorgens, Joseph: Bilateral glenoid hypoplasia, 568  
 Katz, Louis N.: The atherosclerosis problem, 755  
 Keys, Ancel: Diet and atherosclerosis, 206  
 Keys, Ancel: Mode of life and the prevalence of coronary heart disease, 758  
 Kimball, Anne C., Bauer, Henry, and Barr, R. N.: Serological testing for syphilis in Minnesota, 98  
 Kirklin, John W.: Surgical treatment of coronary arterial disease, 570  
 Kucera, S. T.: Teratoma of the recto-sigmoid, 109

## L

Laboratory aid in the diagnosis of lupus erythematosus, 641  
 Laboratory control of anticoagulant therapy, 43  
 Labyrinthine hydrops, 414  
 Larimer, Earl M.: Motor vehicle safety for Minnesota children, 484  
 Larson, Donald M., Hauge, E. T., McKenzie, Charles H., and Duryea, Marbry: Inversion of the uterus immediately following delivery, 700  
 Latts, Elliot M.: Diamox, 184  
 LeMar, John D.: Leukemia or leukemoid reaction? 497  
 Leukemia or leukemoid reaction? 497  
 Levey, Stanley, Benson, Jerrel W., Davis, John H., and Abbott, William E.: Alterations of carbohydrate metabolism following trauma, March suppl., 55  
 Levo-dromoran tartrate, a combination of, and a new narcotic antagonist, Preoperative use of, 637  
 Lewis, F. John: Hypothermia in cardiac and general surgery, 77  
 Lewis, Lena A.: The lipoprotein system, 775  
 Life insurance looks at the arteriosclerosis problem, 736

# INDEX TO VOLUME 38

- Limitations of the Widal test, 189
- Lipoprotein metabolism in the etiology of atherosclerosis, 767
- Lipoprotein system, The, 775
- Lipscomb, Paul R.: Management of recent injuries of the hand, 299
- Liver, Hemobilia following blunt trauma to the (case report), 333
- Love, J. Grafton, and Blackburn, Charles M.: Association of intracranial meningioma with pituitary adenoma (case report), 335
- Lowe, Charles U.: Pediatric electrolyte problems, March suppl. 9
- Lundeberg, Karl R., Gunlaugson, F. G., and Roberts, Jean: A study of cancer mortality in Minneapolis, Minnesota, 551
- Lundy, John S.: Will analgesia evolve from a century of anesthesia? 682
- Lung, Cytologic studies in the diagnosis of cancer of the, 704
- Lupus erythematosus, Laboratory aid in the diagnosis of, 641
- Lymphoma, Enigmas in, 674

## Laboratory Aids

- Acute myasthenia gravis and benign thymoma, 338
- Blood coagulation, 571
- Carcinoma *in situ* of the uterine cervix, 331
- Cytologic studies in the diagnosis of cancer of the lung, 704
- Diagnostic enigmas of diseases of bone, 111
- Diagnosis of pancreatitis by laboratory methods, The, 430
- Exfoliative cytology: a realistic appraisal, 812
- Functioning ovarian tumors, 245
- Laboratory aid in the diagnosis of lupus erythematosus, 641
- Laboratory control of anticoagulant therapy, 43
- Leukemia or leukemoid reaction? 497
- Limitations of the Widal test, 189
- Pathology has emerged from the "deadhouse", 937

## Letters to the Editor

- Hess, Arthur E. (standardization of medical report forms used by agencies), 824
- Kahlenberg, Herman H. (criticism of chemical formula contained in article), 823
- Plass, Herbert (criticism of Salk vaccine publicity), 823
- Thompson, Donald C. (Calvert School for the education of home-bound children of elementary school age), 284

## Mc

- McDermott, Robert, Berkwitz, N. J., and Hodges, Allen: Psychiatric out-patient treatment, 633
- McDonald, John R.: Cytologic studies in the diagnosis of cancer of the lung, 704
- McDonald, John R.: Exfoliative cytology: a realistic appraisal, 812
- McGill, James Warren: Death in utero, 701
- McKenzie, Charles H.: Hysterectomies, 451
- McKenzie, Charles H., and Swain, Francis M.: Diabetes insipidus and pregnancy, 809
- McKenzie, Charles H., Duryea, Marbry, Larson, Donald M., and Hauge, E. T.: Inversion of the uterus immediately following delivery, 700
- McKinlay, C. A.: Clinical observations related to pulmonary eosinophilia, 128
- McMillan, G. C.: Pleomorphism of the lesions of arteriosclerosis, 746
- McNear, George R., Jr.: Meconium peritonitis, 90

## M

- Malmros, Haqvin, and Wigand, Gerhard: Treatment of hypercholesteremia, 864
- Maloney, William F.: Challenge of arteriosclerosis to medical education, 731
- Management of acute abdominal diseases, 315
- Management of recent injuries of the hand, 299
- Mann, Frank D.: Laboratory control of anticoagulant therapy, 43
- Margolis, Philip M., and Schiele, Burtrum C.: Value of succinylcholine chloride in electroconvulsive therapy, 1
- Marks, Herbert H., and Shepard, William P.: Life insurance looks at the arteriosclerosis problem, 736
- Marmorston, Jessie, Hoffman, Olive, Sobey, Harry, and Starr, Paul: Urinary estrogen and serum protein-bound iodine levels, 800
- Maternal mortality, Influence of anesthesia on, 623
- Maternal mortality study, Minnesota, 9
- Meconium peritonitis, 90
- Medical aspects of peptic ulcer, 141
- Medical emergencies in myocardial infarction, 888
- Medical partnerships, 93
- Medico-legal relations, 228
- Meningioma, intracranial, Association of, with pituitary adenoma (case report), 335
- Metabolism, Cholesterol, 779
- Metabolism, Lipoprotein, in the etiology of atherosclerosis, 767
- Miller, Fletcher, and Brown, E. B., Jr.: Clinical importance of hypercapnia, 602
- Miller, Z. R.: Multiple sclerosis, 237
- Milliequivalent as a unit of measure in the interpretation and correction of electrolyte disturbances, The, March suppl., 1
- Milliequivalents, Why? 148
- Minnesota maternal mortality study, 9
- Mitchell, Berton D.: Blood volume studies in gastrointestinal hemorrhage, 172
- Mortality of life and the prevalence of coronary heart disease, 758
- Mortality, cancer, A study of, in Minneapolis, Minnesota, 551
- Mortality, infant, Can we further decrease? 559
- Mortality, maternal, Influence of anesthesia on, 623
- Mortality study, Maternal, Minnesota, 9
- Motor vehicle safety for Minnesota children, 484
- Mucosa, gastric, Biopsy studies of the, 268
- Multiple sclerosis, 237
- Murphy, Thomas O., and Aust, J. Bradley: Use of greater saphenous vein autographs in reconstruction of segmental arterial occlusions, 918
- Myhre, James: Medical aspects of peptic ulcer, 141
- Myocardial infarction, Medical emergencies in, 888

## Medical Economics

- AMA comments on Hoover report, 252
- AMA officials hear polio report, 439
- AMA reviews legislation status, 345
- AMA session: democracy in action, 508
- AMA studies medical care economics, 820
- AMEF reports state standings, 52
- America called medical magnet, 821
- Business has an interest in health, 204
- Charges made against more health insurance firms, 440
- Compulsory health insurance again introduced, 203
- Compulsory health insurance enacted for Sweden, 122
- Congress adjourns with health bills pending, 653
- County society studies doctors' estates, 944
- Doctors, union fund sign up, 714
- Economist forecasts U. S. in 1960, 510
- Federal health budget to reach over \$2 billion, 51
- Fee advice for young physicians, 585
- Folsom asks more funds for medical research, 946
- Government inefficiency seen in Great Britain, 714
- Graduate medical education shows big gains, 945

# INDEX TO VOLUME 38

Group clinic regulation upheld, 440  
 Health message shows little change, 202  
 Health report on state relations issued, 653  
 Hobby says AMA will accept reinsurance, 254  
 Hoover commission reports on medical services, 252  
 Insurance company offers cancer rider, 440  
 JAMA asks tax-supported medical schools relax restrictions, 51  
 "Just keeping up" takes time, 253  
 Labor secretary urges expansion of health insurance, 53  
 Legion commander addresses M.D.'s, 123  
 M.D. shortage is a fading specter, 204  
 Medical costs survey notes trends, 944  
 More funds urged for FDA, 583  
 National Board notes exam requirements, 347  
 New group to study health plans, 122  
 PHS to handle Indian medical care responsibility, 655  
 President's budget is extensive, expensive, 203  
 President cited for medical education work, 52  
 Public service explained by Doctor Hess, 123  
 Reinsurance to be reintroduced, 53  
 Report shows United States cost of sickness, 124  
 Rural health leaders gather, 253  
 Secretary indicates change of heart, 713  
 Social security, OASI figures notes, 946  
 Standard health insurance plan proposed for U.S. workers, 203  
 State seventh high in old age assistance, 583  
 Stop abusing hospital insurance, 584  
 Suggestions on joint commission on accreditation wanted, 945  
 Surplus property sought for health facilities, 253  
 Survey shows public likes M.D.'s, 819  
 Tax deferment bills make slow progress, 346  
 Two world medical groups discussed, 655  
 Vets medical care to get new appraisal, 583

## Minnesota State Board of Medical Examiners

Ex-convict (Charles A. Allen) masquerading as doctor of medicine sentenced, 711  
 First conviction under Minnesota physical therapy law (Edith Lundeen), 510  
 License of Kenneth L. Kelsey suspended for five years, 441  
 License of Arthur F. Sether suspended for three years, 208  
 Minneapolis midwife sentenced for making false birth certificate (Lillian Twedt), 952  
 Minneapolis woman sentenced for abortion (Alma Dora Peterson), 530  
 Minneapolis man sentenced on abortion charge (William V. Smith), 510  
 Physicians licensed in 1954, 259  
 Saint Paul woman (Assunda Willner) sentenced for abortion, 587

## Miscellaneous

Abstracts, (September) xxxv  
 Group disability insurance, (July) xxiii  
 Minnesota State Medical Association—House of Delegates—Summary of Proceedings, May 22 and 23, 1955, (August) xxiv  
 X-ray motion pictures aid in study of swallowing process, (July) xxxi

## N

National Heart Institute, Role of the, in meeting the challenge of arteriosclerosis, 734  
 Neck, Differential diagnosis of tumors of the, 293  
 Nerenberg, Samuel T.: The diagnosis of pancreatitis by laboratory methods, 430  
 Neurodermatitis, 291  
 New hydrocortisone for intra-articular use, A, 408  
 Newman, Elliot V.: Quantitative electrocardiography, 374

Niknejad, Ismail, Aurelius, J. Richards, and Peterson, Donald H.: Retroperitoneal cavernous hemangioma associated with hemangiomas of the skin in a newborn, 32  
 Nursing in Minnesota, Facts about, 38

## O

Observations on the history of the bronchopulmonary segments, 597  
 Obstetric hemorrhage, Foibles and pitfalls in, 684  
 Obstruction, Intestinal, due to inflammatory strictures, 481  
 Obstruction of the bowel, Complete, in the newborn, 165  
 Occlusions, segmental arterial, Use of greater saphenous vein autographs in reconstruction of, 918  
 Occlusive arterial disease—its management by the use of homografts, 912  
 Occlusive arterial disease—its management by thromboendarterectomy, 904  
 Older patients, Digestive ailments of, 309  
 Oliver, M. F., and Boyd, G. S.: Coronary atherogenesis—an endocrine problem? 794  
 Osborn, John E.: Influence of anesthesia on maternal mortality, 623  
 Ott, Harold A.: Foibles and pitfalls in obstetric hemorrhage, 685  
 Ovarian tumors, Functioning, 245  
 Owen, Charles A., Jr.: Blood coagulation, 571  
 Owens, Frederick, Jr., and Hay, Lyle J.: Transplantation of duct of Wirsung in chronic pancreatitis, 411

## P

Page, Irvine H.: Strategy and tactics of research in arteriosclerosis, 743  
 Palmerton, E. S.: Visual problems of patients who have unilateral cataract operations, 420  
 Pancreatitis, chronic, Transplantation of duct of Wirsung in, 411  
 Pancreatitis, The diagnosis of, by laboratory methods, 430  
 Parotid salivary gland, Tumors of the, 476  
 Partnerships, Medical, 93  
 Pathogenesis of atherosclerosis, Hormonal factors in the, 788  
 Pathogenesis of hyaline membrane disease of the newborn, The, 514  
 Pathology has emerged from the "deadhouse," 937  
 Pease, Gertrude L.: Laboratory aid in the diagnosis of lupus erythematosus, 641  
 Pediatric electrolyte problems, March suppl., 9  
 Peltier, Leonard F.: Fractures of the pelvis, 563  
 Pelvis, Fractures of the, 563  
 Penis, Giant condyloma (verruca) simulating carcinoma of the, 423  
 Peptic ulcer, Medical aspects of, 141  
 Peritonitis, Meconium, 90  
 Perry, John F., Jr., Yonehiro, Earl G., and Smith, Grafton A.: Intestinal obstruction due to inflammatory strictures, 481  
 Peterson, Donald H., Niknejad, Ismail, and Aurelius, J. Richards: Retroperitoneal cavernous hemangioma associated with hemangiomas of the skin in a newborn, 32  
 Physical therapy for painful shoulder, 556  
 Pierce, Jack R.: Can we further decrease infant mortality? 559  
 Pituitary adenoma, Association of intracranial meningioma with (case report), 335  
 Plasma volume expanders, Blood transfusions and, March suppl., 48  
 Plastic replacement of diseased arterial segments, 927  
 Pleomorphism of the lesions of arteriosclerosis, 746  
 Pleural effusion, Idiopathic, 613  
 Poliomyelitis complicating pregnancy, 668  
 Polypoid rhabdomyosarcoma of the bladder: sarcoma botryoides, 215

# INDEX TO VOLUME 38

Potassium deficiency, Relation of alkalosis to, March suppl., 4  
 Practical approach to the treatment of tetanus, A, 397  
 Precautions in the use of cortisone for treatment of rheumatic diseases, 304  
 Pregnancy, Diabetes insipidus and, 809  
 Pregnancy, ectopic, 179  
 Pregnancy, Poliomyelitis complicating, 668  
 Preoperative use of a combination of levo-dromoran tartrate and a new narcotic antagonist, 637  
 Present treatment of subacute bacterial endocarditis, 936  
 Problems of the clinical diagnosis and classification of ventricular hypertrophy (discussion only), 267  
 Proffitt, William E.: Athletic accident benefit plan, 1954-1955, 183  
 Prophylaxis of rheumatic fever, 702  
 Pruritus, Anal, 19  
 Psychiatric aspects of ulcerative colitis, 86  
 Psychiatric illness following gastric resection, 226  
 Psychiatric out-patient treatment, 633  
 Psychoses, Puerperal, 223  
 Puerperal psychoses, 223  
 Pulmonary edema, Acute, 605  
 Pulmonary eosinophilia, Clinical observations related to, 128  
 Pulmonary-function tests, 599

## President's Letter

AMA meeting, The, 507  
 American Medical Education Foundation, 577  
 Annual challenge, The, 49  
 Cornerstone, The, 117  
 County medical society activities, 712  
 In appreciation, 340  
 Legislative review, 438  
 No time for littleness, 943  
 Our 102nd meeting, 247  
 Social security for physicians, 651  
 Something good, 818  
 To give wisely, 196

## Public Health

Duties of the physician in registering births and deaths, 205  
 Guide for medical policies for local public health nursing services, 125  
 Poliomyelitis vaccination in Minnesota, 716  
 Program for professional personnel in national emergencies, 443  
 State dental health program has many phases, 255  
 State plan for distribution of Salk vaccine, 716  
 Tribute to two public health workers, 54

## Q

Quantitative electrocardiography, 874  
 Quinidine, The use of, in clinical medicine, 499

## R

Radical treatment of brain abscess, 547  
 Radioisotope studies of the physiology of calcified tissues, 618  
 Raetz, S. J., and Smith, Richard T.: Histoplasmosis, 531  
 Raudenbush, David W., and Kamman, Gordon R.: Medico-legal relations, 228  
 Recto-sigmoid, Teratoma of the, 109  
 Rectum, Tumors of the colon and, 401  
 Regan, John J., and Rowe, Clarence J.: Psychiatric illness following gastric resection, 226  
 Relation of alkalosis to potassium deficiency, March suppl., 4  
 ReMine, William H.: Management of acute abdominal diseases, 315

Renal insufficiency, Acute, March suppl., 52  
 Resection, gastric, Psychiatric illness following, 226  
 Retroperitoneal cavernous hemangioma associated with hemangiomas of the skin in a newborn, 32  
 Rhabdomyosarcoma, Polypoid, of the bladder: sarcoma botryoides, 215  
 Rheumatic diseases, Precautions in the use of cortisone for treatment of, 304  
 Rheumatic fever, Prophylaxis of, 702  
 Rice, Carl O., and Strickler, J. H.: Clinical aspects of fluid and electrolyte management, 153  
 Rice, Carl O., and Strickler, J. H.: Hyperkalemia and hyperglycemia, 565  
 Roberts, Jean, Lundberg, Karl R., and Gunlaugson, F. G.: A study of cancer mortality in Minneapolis, Minnesota, 551  
 Role of the National Heart Institute in meeting the challenge of arteriosclerosis, 734  
 Rosenow, John H.: Why milliequivalents? 148  
 Rossing, Robert G.: Idiopathic pleural effusion, 613  
 Rowe, Clarence J., and Regan, John J.: Psychiatric illness following gastric resection, 226  
 Russek, Henry I.: Evaluation of status and results of management in coronary heart disease, 891

## Reports and Announcements

AMA Council on Education and Hospitals, 69  
 American Academy of Forensic Sciences, 69  
 American Academy of General Practice, 349  
 American Association of Anatomists, 349  
 American Board of Obstetrics and Gynecology, 134, 283, 444, 950  
 American Cancer Society, 658  
 American College of Chest Physicians postgraduate courses, 590  
 American College of Chest Physicians to hold student essay contest, 727  
 American College of Gastroenterology, 590  
 American Congress of Physical Medicine and Rehabilitation, 283  
 American Dermatological Association annual prize essay contest, 524  
 American Goiter Association award, 590  
 American Hearing Society, 134  
 American Institute of Dental Medicine, 207  
 American Urological Association offers essay awards, 524  
 Ames award contest for gastroenterology, 283  
 Art and hobby show at state meeting, 208  
 Arthritis and Rheumatism Foundation, Minnesota Chapter, 349, 591  
 Assembly in otolaryngology, 444  
 Association of Military Surgeons, 727  
 Continuation courses:  
     Allergy and chest diseases for general physicians, 136  
     Bacteriology and blood bank techniques for medical technologists, 592  
     Cancer detection, 950  
     Cardiovascular diseases for general physicians, 135  
     Clinical chemistry for physicians, 529  
     Clinical dietetics for dietitians, 70  
     Clinical hematology for physicians, 71  
     Emergency surgery for general physicians, 135, 950  
     Eye, ear, nose and throat for general physicians, 950  
     Fractures for general physicians, 657  
     Gastroenterology for general physicians, 727  
     Gynecology for general physicians, 135  
     Introduction to electrocardiology, 284  
     Neurology, 950  
     Obstetrics for general physicians, 826  
     Office psychotherapy in psychosomatic problems, 529  
     Pediatrics for pediatricians, 524  
     Radiology for general physicians, 135  
     Radiology for radiologists, 592  
     Recent advances in internal medicine for internists, 70, 950

# INDEX TO VOLUME 38

Surgery for general surgeons, 284  
 Techniques in general practice, 529  
 Tuberculosis for lay persons, 529  
 Course in clinical pathology and pathology of parasitic diseases, 207  
 Crippled Children Clinics, 658  
 Discontinuation of the rheumatic fever program, crippled children services, Department of Welfare, 524  
 Essay award contest (American College of Chest Physicians), 70  
 Family doctors' days, 69, 134  
 Industrial health course, 657  
 Industrial medicine course, 444  
 International College of Surgeons, 207  
 International Congress on Diseases of Chest, 826  
 Lectures and discussions on current medical problems, 70  
 Licensure examination, 136  
 Lyon-Lincoln Society clinic course, 727  
 Medical meetings, 69, 134, 207, 283, 349, 444  
 Mediclinic of Minnesota, 826  
 Mental health grant, 135  
 Minnesota Academy of General Practice, 591, 657  
 Minnesota Academy of Medicine:  
   Meeting of March 10, 1954, 128  
   Meeting of April 14, 1954, 267  
   Meeting of May 12, 1954, 275  
   Meeting of October 13, 1954, 514  
   Meeting of November 10, 1954, 592  
 Minnesota Academy of Occupational Medicine and Surgery, 524  
 Minnesota Heart Association, 208, 591  
 Minnesota League for Nursing, 283  
 Minnesota Medical Foundation, 350  
 Minnesota Obstetrical and Gynecological Society, 349  
 Minnesota Society of Neurology and Psychiatry, 70, 349  
 Minnesota State Medical Association:  
   Preliminary program—102nd annual meeting, 256  
   Roster, 358  
   Summary of proceedings, (August) xxiv  
 Minnesota symposium on arteriosclerosis, 444  
 Minnesota Tuberculosis and Health Association, 70  
 National hospital week, 134  
 New Orleans Graduate Medical Assembly, 826  
 Northern Minnesota Medical Association, 591  
 Northfield City Hospital, 135  
 Pan American Medical Association, 208  
 Physician pilots organize, 135  
 Postgraduate course on diseases of the chest, 70  
 Public health radio-TV series, 208  
 Range Medical Society elects, 71  
 St. Louis County Society meets, 71, 349  
 Safety clinic held in Sauk Centre, 71  
 Schering award competition for medical students, 283  
 Seminar in ophthalmology and otolaryngology, 826  
 Survey of postgraduate medical education, 208  
 Tape recordings on heart disease, 826  
 Technical editors and writers needed, 284  
 Tri-county Medical Society election, 71  
 Trudeau School of Tuberculosis, 284  
 Twin Cities Diabetes Association, 727  
 Wabasha County Society, 950  
 Wangenstein Anniversary program, 591  
 Workshop in medical writing, 657  
 World Medical Association journalism meeting, 444

## S

Sadler, William P., and Bergquist, James R.: Poliomyelitis complicating pregnancy, 668  
 Safety, Motor vehicle, for Minnesota children, 484  
 Salivary gland, parotid, Tumors of the, 476  
 Saphenous vein autographs, greater, Use of, in reconstruction of segmental arterial occlusions, 918  
 Sarcoma botryoides, Polypoid rhabdomyosarcoma of the bladder:, 216  
 Sauvage, Lester R.: Healing and fate of arterial homographs, 916

Scarborough, William R.: Ballistocardiogram in the diagnosis of coronary atherosclerosis, 880  
 Schiele, Burtrum C., and Margolis, Philip M.: Value of succinylcholine chloride in electroconvulsive therapy, 1  
 Schizophrenia, Hypertensive encephalopathy versus, 636  
 Sclerosis, Multiple, 237  
 Seldin, Donald: Development and correction of electrolyte disturbances associated with salt retention, March suppl., 21  
 Serological testing for syphilis in Minnesota, 98  
 Shepard, William P., and Marks, Herbert H.: Life insurance looks at the arteriosclerosis problem, 736  
 Shoulder, painful, Physical therapy for, 556  
 Shumacker, Harris B., Jr.: Plastic replacement of diseased arterial segments, 927  
 Simonson, Ernst: Electrocardiogram in coronary heart disease, 871  
 Simonton, Kinsey M.: Hearing loss in children, 5  
 Sinykin, Melvin B., and Barr, Maxwell M.: Gynecological cancer detection, 174  
 Sjoding, J. Donald: Indications and contraindications for adenotonsillectomy, 458  
 Skin diseases, Topical hydrocortisone in the treatment of, 404  
 Smith, Baxter A., Jr.: Polypoid rhabdomyosarcoma of the bladder: sarcoma botryoides, 215  
 Smith, Grafton A., Perry, John F., Jr., and Yonehiro, Earl G.: Intestinal obstruction due to inflammatory strictures, 481  
 Smith, Richard T., and Raetz, S. J.: Histoplasmosis, 531  
 Smith, William T., and Fansler, Walter A.: Tumors of the colon and rectum, 401  
 Snell, Albert M.: Digestive ailments of older patients, 309  
 Sobel, Harry, Starr, Paul, Marmorston, Jessie, and Hoffman, Olive: Urinary estrogen and serum protein-bound iodine levels, 800  
 Socialized medicine, "Ideal," 538  
 Society, The county medical, 665  
 Sommers, Ben: Problems of the clinical diagnosis and classification of ventricular hypertrophy (discussion only), 267  
 Sommers, Ben: The value of the electrocardiogram in diagnosis, 640  
 Southern Minnesota Medical Association, The, 220  
 Starr, Paul, Marmorston, Jessie, Hoffman, Olive, and Sobel, Harry: Urinary estrogen and serum protein-bound iodine levels, 800  
 Stilwell, George G.: Pathology has emerged from the "deadhouse", 937  
 Storsteen, Kenneth A., and Young, Thomas O.: Cancer of the thyroid, 468  
 Strategy and tactics of research in arteriosclerosis, 743  
 Strickler, J. H., and Rice, Carl O.: Clinical aspects of fluid and electrolyte management, 153  
 Strickler, J. H., and Rice, Carl O.: Hyperpotassemia and hyperglycemia, 565  
 Study of cancer mortality in Minneapolis, Minnesota, A, 551  
 Succinylcholine chloride, Value of, in electroconvulsive therapy, 1  
 Sudden, apparently unexplained deaths during infancy, 41  
 Suffocation, a killer of children, 107  
 Sugar, amino acids and, Vehicles and volume, with special reference to, March suppl., 26  
 Surgery, cardiac and general, Hypothermia in, 77  
 Surgical patient, Fluid and electrolyte requirements of the, as influenced by the post-traumatic response, March suppl., 36  
 Surgical treatment of aneurysms of arteriosclerotic origin, 922  
 Surgical treatment of coronary arterial disease, 570  
 Swain, Francis M., and McKenzie, Charles H.: Diabetes insipidus and pregnancy, 809  
 Swenson, A. O.: The county medical society, 665  
 Syphilis, Serological testing for, in Minnesota, 98

Seminar

Diamox, 184  
Multiple sclerosis, 237

T

Technique and interpretation of the vaginal examination, The, 323  
Teratoma of the recto-sigmoid, 109  
Tetanus, 393  
Tetanus, A practical approach to the treatment of, 397  
Three beginnings, founded in the faith, 696  
Thrombo-endarterectomy, Occlusive arterial disease—its management by, 904  
Thyroid, Cancer of the, 468  
Tissues, calcified, Radioisotope studies of the physiology of, 618  
Tobian, Louis: Hypertension and atherosclerosis, 784  
Topical hydrocortisone in the treatment of skin diseases, 404  
Transplantation of duct of Wirsung in chronic pancreatitis, 411  
Trauma, Alterations of carbohydrate metabolism following, March suppl., 55  
Treatment of anemia, The, 327  
Treatment of hypercholesteremia, 864  
Tudor, Robert B.: Sudden, apparently unexplained deaths during infancy, 41  
Tumors, Functioning ovarian, 245  
Tumors of the colon and rectum, 401  
Tumors of the neck, Differential diagnosis of, 293  
Tumors of the parotid salivary gland, 476

U

Ulcer, peptic, Medical aspects of, 141  
Ulcerative colitis, Psychiatric aspects of, 86  
Upper extremity, Fractures of the, in children, 296  
Urinary estrogen and serum protein-bound iodine levels, 800  
Use of greater saphenous vein autographs in reconstruction of segmental arterial occlusions, 918  
Use of quinidine in clinical medicine, The, 499  
Utendorfer, Robert W.: Tumors of the parotid salivary gland, 476  
Utero, Death in, 701  
Uterus, Inversion of the, immediately following delivery, 700

V

Vaginal examination, The technique and interpretation of the, 323  
Value of succinylcholine chloride in electroconvulsive therapy, 1  
Value of the electrocardiogram in diagnosis, 640  
Van Bergen, Frederick H.: Hexamethonium-induced hypotension, 573

Varco, Richard L.: Challenge of arteriosclerosis to surgeons, 902  
Vehicles and volume with special reference to amino acids and sugar, March suppl., 26  
Vein autographs, greater saphenous, Use of, in reconstruction of segmental arterial occlusions, 918  
Ventricular hypertrophy, Problems of the clinical diagnosis and classification of (discussion only), 267  
Visual problems of patients who have unilateral cataract operations, 420

W

Ward, L. Emmerson: Precautions in the use of cortisone for treatment of rheumatic diseases, 304  
Wartman, William B.: Factors other than cholesterol in arteriosclerosis, 749  
Water safety for Minnesotans, 428  
Watkins, Charles H.: The treatment of anemia, 327  
Watt, James: Role of the National Heart Institute in meeting the challenge of arteriosclerosis, 734  
Weisman, Samuel A.: The use of quinidine in clinical medicine, 499  
Wells, Arthur H.: Diagnostic enigmas of diseases of bone, 111  
White, Paul D.: The coronaries through the ages, 801  
Why milliequivalents? 148  
Widal test, Limitations of the, 189  
Wigand, Gerhard, and Malmros, Haqvin: Treatment of hypercholesteremia, 864  
Will analgesia evolve from a century of anesthesia? 682  
Wirsung, Transplantation of duct of, in chronic pancreatitis, 411  
Wylie, Edwin J.: Occlusive arterial disease—its management by thrombo-endarterectomy, 904

Woman's Auxiliary

Clarkfield holds Health Day, 351  
County auxiliaries report health projects, 285  
County presidents report activities, 728  
Hennepin Auxiliary convention hostesses, 285  
International Health Organizations—Part I, 351  
Message from the president, 658  
Mid-winter meeting well attended, 209  
National Auxiliary holds conference, 951  
Ramsey Auxiliary reports activities, 136, 209, 285, 351  
Ramsey Auxiliary elects officers, 445  
Ramsey wives plan fall fashion festival, 592  
State Auxiliary holds fall meeting, 951  
Working together for health and safety, 68

Y

Ylvisaker, R. S.: Biopsy studies of the gastric mucosa, 268  
Yonehiro, Earl G., Smith, Grafton A., and Perry, John F., Jr.: Intestinal obstruction due to inflammatory strictures, 481  
Young, Thomas O., and Storsteen, Kenneth A.: Cancer of the thyroid, 468

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